“A CLINICAL COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN BRACHIAL PLEXUS BLOCK BY SUPRACLAVICULAR APPROACH”

Dissertation submitted in partial fulfilment of the

Requirement for the award of the Degree of

DOCTOR OF MEDICINE - BRANCH X

ANAESTHESIOLOGY

APRIL 2015

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

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DECLARATION

I, **Dr.B.SUNDARI,** declare that the dissertation titled **"A CLINICAL COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN BRACHIAL PLEXUS BLOCK BY SUPRACLAVICULAR APPROACH"** has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D. Degree, Branch X (ANAESTHESIOLOGY) degree Examination to be held in April 2015.

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PROTOCOL TITLE: A clinical comparative study between dexmedetomidine and clonidine as an adjuvant to bupivacaine in brachial plexus block by supraclavicular approach

NAME OF PRINCIPAL INVESTIGATOR: Dr. B.Sundari
DESIGNATION OF PRINCIPAL INVESTIGATOR: Resident in Anaesthesiology
DEPARTMENT & INSTITUTION: Department of Anaesthesiology, Tirunelveli Medical College

Dear Dr. B.Sundari, *The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 28.12.13.*

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☑
2.	Study Protocol	☑
3.	Department Research Committee Approval	☑
4.	Patient Information Document and Consent Form in English and Vernacular Language	☑
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☑
7.	Curriculum Vitae of the Principal Investigator	☑
8.	Insurance /Compensation Policy	☑
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☑
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☑
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

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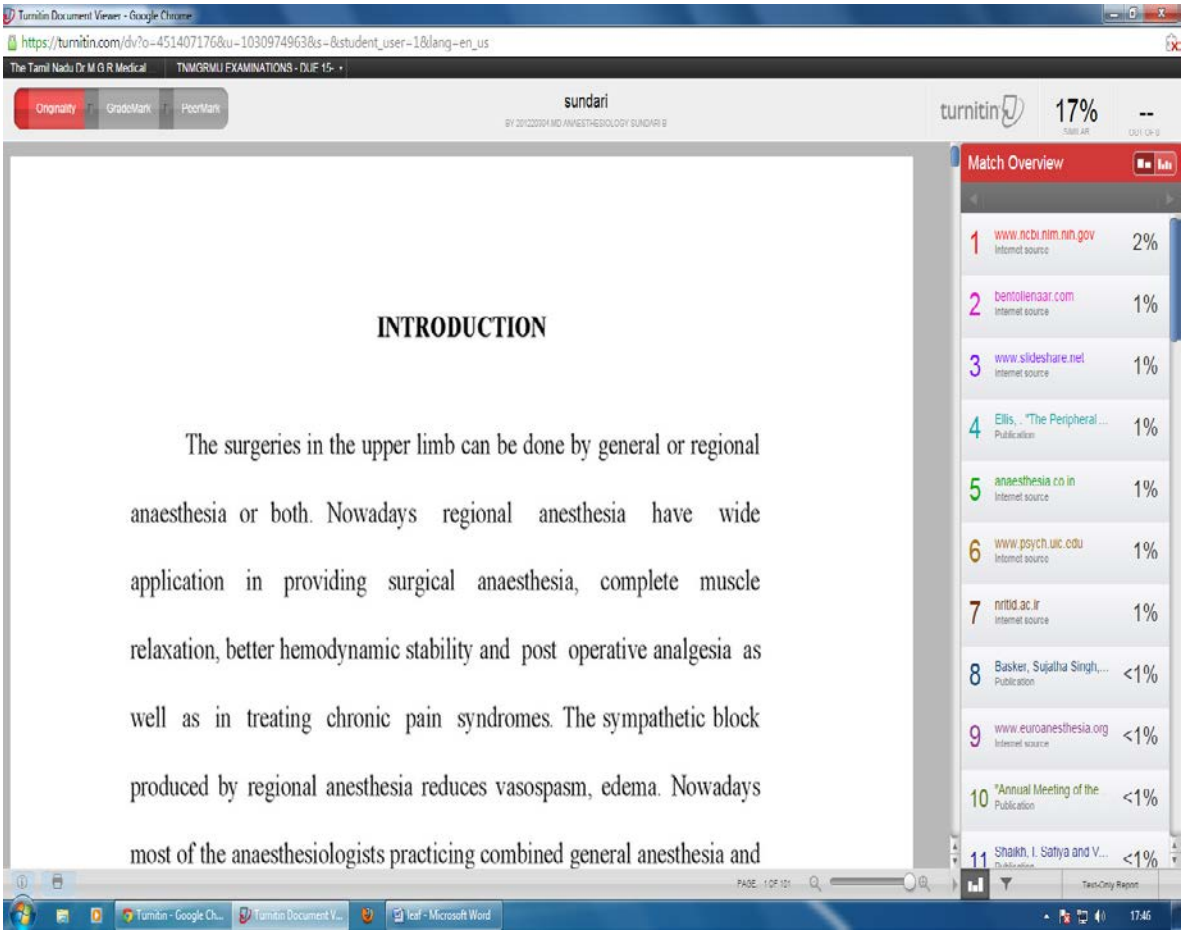
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INTRODUCTION
The surgeries in the upper limb can be done by general or regional anaesthesia or both. Nowadays regional anesthesia have wide application in providing surgical anaesthesia, complete muscle relaxation, better hemodynamic stability and post operative analgesia as well as in treating chronic pain syndromes. The sympathetic block produced by regional anesthesia reduces vasospasm, edema. Nowadays most of the anaesthesiologists practicing combined general anesthesia and
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A CLINICAL COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND CLONIDINE AS AN ADJUVANT TO BUPIVACAINE IN BRACHIAL PLEXUS BLOCK BY SUPRACLAVICULAR APPROACH

AIM OF THE STUDY

Recently alpha 2 agonists are playing a vital role as an adjuvant in neuraxial block and peripheral nerve block. The purpose of this study is to compare the efficacy of Dexmedetomidine and Clonidine with Bupivacine in brachial plexus block by supraclavicular approach.

MATERIAL AND METHODS :

It is a prospective randomised single blinded study, conducted in unilateral upper limb surgeries under brachial plexus block. Patients were divided into two groups as Group B&C, GroupB&D, Group B&C (N=30) – 35 ml of 0.357% Bupivacaine with Clonidine 2microgm/kg. Group B&D (N=30) - 35 ml of 0.357% Bupivacaine with Dexmedetomidine 2microgm/kg.

INCLUSION CRITERIA

- ASA I, II
- Age 20 to 50
- Unilateral upper limb orthopaedic surgeries
- Both sexes

EXCLUSION CRITERIA

- ❖ Patient Refusal
- ❖ Patient on adrenoreceptor agonist or antagonist therapy.
- ❖ Suspected coagulopathy
- ❖ Infection at the site of block
- ❖ History of respiratory, cardiac, hepatic or renal failure.
- ❖ Patients with medical complications like severe anemia, severe hypovolemia, shock, septicemia.
- ❖ Allergy to local anaesthetics and study drug.
- ❖ Pregnant women.

Objectives:

- ∗ Sensory block- onset time
- ∗ Motor block-onset time
- ∗ Complete duration of sensory and motor block
- ∗ Total duration of analgesia
- ∗ Adverse effects

RESULTS:

Comparison of quality of block

Quality	**Mean**	**SD**	**p value**	**t value**	
Group BC	3.13	0.82	< 0.001	4.52	Significant
Group BD	3.87	0.35			

Bupivacaine dexmedetomidine group has better quality than bupivacaine clonidine group.

Comparison of onset time of sensory block(minutes)

	Mean	**SD**	**p value**	**t value**	
Group BC	8.47	1.04	< 0.001	17.19	Significant
Group BD	4.7	0.59			

The mean time for onset of sensory block in Group BD was 4.7 minutes which was lower than Group BC -8.47 minutes. This was statistically significant($p<0.05$)

Comparison of onset time of motor block between two groups

OTMB	**Mean**	**SD**	**p' value**	**t value**	
Group BC	13.1	1.42	< 0.001	11.32	Significant
Group BD	9.63	0.89			

The mean time for onset of motor block in Group BD was 9.63 minutes which was lower than Group BC -13.1minutes.This was statistically significant($p<0.05$).

Comparison of total duration of sensory block between two groups (mt)

TDSB	**Mean**	**SD**	**p' value**	**t value**	
Group BC	319.1	32.74	< 0.001	25.89	
Group BD	537.8	32.67			Significant

The mean time for total duration of sensory block in Group BD was 537.8minutes. This was higher than the Group BC -319.1minutes.It was statistically significant($p<0.05$).

Comparison of total duration of motor block between two groups

TDMB	Mean	SD	p' value	Tvalue	
Group BC	222.23	17.84	< 0.001	40.27	Significant
Group BD	466.87	28.08			

The mean time for total duration of motor block in Group BD was 466.87minutes. This was higher than in Group BC 222.23 minutes. It was statistically significant($p<0.05$).

Comparison of total duration of analgesia between two groups

DOA	Mean	SD	p value	t value	
Group BC	375.23	32.6	< 0.001	32.55	Significant
Group BD	666.27	36.54			

The total duration of Analgesia in Group **B**D was 666.27 minutes. This was higher than in Group BC – 375.23 minutes. It was statistically significant. ($p<0.05$).

SUMMARY

In adult patients undergoing orthopaedic forearm and hand surgeries under brachial plexus block, the addition of 2μg/kg of dexmedetomidine to 35 ml of bupivacaine (0.357%) produces a shorter onset time for sensory and

motor blockade. It also prolongs the duration of sensory and motor blockade. Postoperatively the duration of analgesia is prolonged with minimal reduction in pulse rate,blood pressure.

CONCLUSION

The addition of Dexmedetomidine (2μg/kg) to bupivacaine (0.357%) in brachial plexus block by supraclavicular approach results in a shorter onset time for sensory and motor blockade, prolongs the duration of sensory and motor blockade and also the duration of analgesia.

KEYWORDS : Supraclavicular block, Bupivacaine, Dexmedetomidine, Clonidine.

INTRODUCTION

The surgeries in the upper limb can be done by general or regional anaesthesia or both. Nowadays regional anesthesia have wide application in providing surgical anaesthesia, complete muscle relaxation, better hemodynamic stability and post operative analgesia as well as in treating chronic pain syndromes. The sympathetic block produced by regional anesthesia reduces vasospasm, edema. Nowadays most of the anaesthesiologists practicing combined general anesthesia and regional anesthesia in paediatric patients. It reduces the anesthetic requirements and provides smooth extubation.

Regional anaesthesia has several advantages in the postoperative period compared with general anaesthesia including decreased sedation, decreased nausea and vomiting, early discharge from the recovery room and a smooth transition to pain control as the block effects gradually dissipate.

Brachial plexus provide sensory innervations of the upper limb. William halsted first demonstrated the brachial plexus block by axillary approach.[1] There are various available approaches and techniques in brachial plexus blockade.

These include

a) Interscalene approach

b) Supraclavicular approach

c) Parascalene approach

d) Axillary approach

e) Infraclavicular approach

LOCAL ANAESTHETICS

These are the drugs that block the conduction of impulses in the electrically excitable tissues. Local anaesthetics provide anaesthesia and analgesia by blocking the transmission of pain sensation along the nerve fibres. They are classified into

1. Aminoamide group (Lignocaine, bupivacaine, levobupivacaine etc)
2. Amino ester group (cocaine, Chloroprocaine, procaine, tetracaine)

Bupivacaine is the commonly used local anaesthetic agent. It is a racemic mixture with two enantiomers, levobupivacaine, S (-) isomer and dextrobupivacaine, R(+)isomer.

ADJUVANTS

Adjuvants are added to local anaesthetic agents to

- Prolong the duration of anaesthesia and analgesia
- Reduces the dose requirement
- Reduces the incidence of toxic effects(2)

Various adjuvants like morphine, fentanyl, sufentanil, dexamethasone, midazolam, ketamine, neostigmine, sodabicarbonate are added to local anesthetic agents. Alpha 2 receptor agonists clonidine and dexmedetomidine are of new interest in regional anaesthesia because of their better haemodynamic stability, sedation and longer duration of postoperative analgesia.

Adjuvants are administered by various routes like epidural, intrathecal and intravenous.

DEXMEDETOMIDINE

Alpha 2 adrenergic receptor agonist dexmedetomidine gain the focus of interest for its sedative, analgesic, perioperative sympatholytic and hemodynamic stabilizing properties. Dexmedetomidine is a new highly selective alpha 2 adrenergic receptor agonist[(3).] FDA approved dexmedetomidine as an ICU sedation for mechanical ventilation[(4).] Nowadays new researches are going on about dexmedetomidine as an

excellent adjuvant in neuraxial blocks, peripheral nerve blocks and intravenous regional anaesthesia. Dexmedetomidine improves the quality of anaesthesia by means of fast onset, prolonged duration with sedative effect. It provides excellent post operative analgesia, when compared to other adjuvants.

AIM OF THE STUDY

Recently alpha 2 agonists are playing a vital role as an adjuvant in neuraxial block and peripheral nerve block. The purpose of this study is to compare the efficacy of Dexmedetomidine and Clonidine with Bupivacine in brachial plexus block by supraclavicular approach.

MATERIAL AND METHODS :

It is a prospective randomised single blinded study, conducted in unilateral upper limb surgeries under brachial plexus block. Patients were divided into two groups as Group B&C, GroupB&D, Group B&C (N=30) – 35 ml of 0.357% Bupivacaine with Clonidine 2microgm/kg. Group B&D (N=30) - 35 ml of 0.357% Bupivacaine with Dexmedetomidine 2microgm/kg.

Objectives:

a) Sensory block- onset time
b) Motor block-onset time
c) Complete duration of sensory and motor block
d) Total duration of analgesia
e) Side effects

REVIEW OF LITERATURE

Swami SS et al(5) studied the efficacy of dexmedetomidine and clonidine with bupivacaine in brachial plexus block by supraclavicular approach. They found that dexmedetomidine increases the duration of motor and sensory block with better quality and better post operative analgesia when compared to clonidine

Rachana G et al[6] studied about dexmedetomidine with bupivacaine in brachial plexus block by supraclavicular approach. They concluded that dexmedetomidine provided longer duration of motor and sensory block, increased duration of post operative analgesia and better hemodynamic stability when added with bupivacaine

Sandhya agarwal, et al[7] compared dexmedetomidine with bupivacaine in brachial plexus block by supraclavicular approach. They concluded that dexmedetomidine hastens the onset time, increases the sensory and motor block duration and post operative analgesia.

Ammar AS et al [8] studied the effects of dexmedetomidine with bupivacaine in brachial plexus block by infraclavicular approach. The result was dexmedetomidine enhances the sensory and motor block onset time, increases the duration of analgesia, increases the sensory and motor

blockade duration, produce less VRS (verbal response scale) pain scores and reduces supplemental opioid requirements when added with bupivacaine

Jang ho song et al [9] studied the effect of dexmedetomidine and epinephrine when added to 1%mepivacaine in infraclavicular brachial plexus block. They concluded that dexmedetomidine is a better alternative than epinephrine.

JE kim et al [1p0] studied the effects of dexmedetomidine with bupivacaine intrathecally in TURP surgery. They concluded that dexmedetomidine produces fast onset, increases the sensory block duration and post operative analgesia, but recovery of motor block could be delayed.

Deepika shukla et al[11] studied the effects of dexmedetomidine and magnesium sulphate intrathecally with bupivacaine. They concluded that dexmedetomidine has rapid onset and prolonged duration than magnesium sulphate.

Rancourt et al [12] evaluated the effect of dexmedetomidine with ropivacaine in posterior tibial nerve block. They conclude that sensory blockade is increased by dexmedetomidine.

Cengiz Kaya et al [13] compared the effect of dexmedetomidine premedication intra muscularly on hemodynamics and stress response. They conclude that dexmedetomidine premedication reduces the dose of opioid requirement in induction and better post operative pain relief. It also reduces the stress response.

Kaygusuz K et al[14] studied the efficacy of adding dexmedetomidine (1μg/kg) to levobupivacaine (0.5%) in axillary block. They concluded that dexmedetomidine shortens the onset time for sensory block , increases the duration of motor and sensory block and extends the post operative analgesia

Esmaoglu et al[15] evaluated the effects of dexmedetomidine (100μg) to levobupivacaine in axillary block. They found that dexmedetomidine decreases the onset time for motor and sensory block, extends the sensory and motor blockade duration and extends the duration of analgesia.

Feroz Ahmad Dar et al(16) did a study about dexmedetomidine added to ropivacaine in brachial plexus block by axillary approach. They concluded that dexmedetomidine shortens the sensory and motor blockade onset time. It also prolongs the duration of sensory and motor blockade and increases the duration of analgesia.

Marhofer et al[17] did a study on the adjuvant action of systemic or perineural dexmedetomidine with ropivacaine in peripheral nerve block. They found that systemic and perineural dexmedetomidine increases the motor block duration by 10% and 60%.

Obayah et al [18] evaluated the effect of adding dexmedetomidine to bupivacaine for post operative analgesia in children who were operated for cleft palate repair. He concluded that adding dexmedetomidine with bupivacaine for peripheral nerve block extends the postoperative analgesia with clinically no relevant side effects.

Bajwa et al (19) studied the efficacy of fentanyl and dexmedetomidine to epidural ropivacaine for lower limb orthopaedic surgeries. They found that dexmedetomidine provides stable hemodynamics, early onset of sensory block, prolonged post operative analgesia, less consumption of local anaesthetics postoperatively and better sedation scores.

Al-mustafa et al [20] did a study of adding dexmedetomidine in lower dose to bupivacaine in spinal anaesthesia for urological procedures. They found that dexmedetomidine produces a dose dependent action in the onset and duration of sensory and motor blockade.

Memis D et al [21] evaluated the efficacy of adding dexmedetomidine to lignocaine in intravenous regional anaesthesia. They found that dexmedetomidine added to lidocaine produces the better quality of anaesthesia and perioperative analgesia without causing side effects.

M.A.Abosedira et al [22] compared the effects of clonidine and dexmedetomidine added to lignocaine in bier' s block. They concluded that dexmedetomidine lignocaine mixture enhances the quality of anaesthesia and improves tourniquet tolerance. It also enhances the intraoperative and postoperative analgesia when compared to clonidine

Solanki S et al[23] compared the effects of dexmedetomidine and clonidine with bupivacaine in trauma patients posted for lower limb surgeries. They observed that dexmedetomidine (5 μg) added to bupivacaine (15 mg) intrathecally provides longer duration of postoperative analgesia than clonidine(50 mcg).

Esmaoglu et al al [24] studied the effects of adding dexmedetomidine to lignocaine in bier's block. They found that dexmedetomidine added to lignocaine causes a better quality of anaesthesia and perioperative analgesia without any side effects.

ANATOMY OF BRACHIAL PLEXUS

The brachial plexus provides innervation of the upper limb. The plexus consists of the roots, trunks, divisons, cords, terminal nerves.

ROOTS :

Roots are formed from the anterior primary rami of C5, C6, C7, C8 and T1. In addition there may be contributions from C4 and T2. If the plexus is formed from C4-C8, it is called as prefixed plexus. If the plexus is formed from T2, then it is called as post fixed plexus. The roots are joined together to form the trunks.

TRUNKS:

- C5and C6 roots join to form the upper trunk
- C7 root forms the middle trunk
- C8 and T1 roots join to form the lower trunk.

DIVISIONS:

Trunks are divided into ventral & dorsal divisions which supply the anterior and posterior aspects of the limb.

CORDS :

- Ventral divisions of the upper and middle trunk unites to form the lateral cord.
- Ventral division of the lower trunk forms the medial cord.
- Dorsal divisions of all the trunks unite to form the posterior cord.

BRANCHES :

Branches from the Root:

1) Long thoracic nerve (C5,C6,C7)

Motor supply- serratus anterior

2) Dorsal scapular nerve

Motor supply-Rhomboids (C5)

Levator scapulae

3) Nerve to subclavius

Branches from the Trunk:

1) Suprascapular Nerve (C5,C6)

Motor supply- supra spinatus & infra spinatus

2) Nerve to Subclavius (C5,C6)

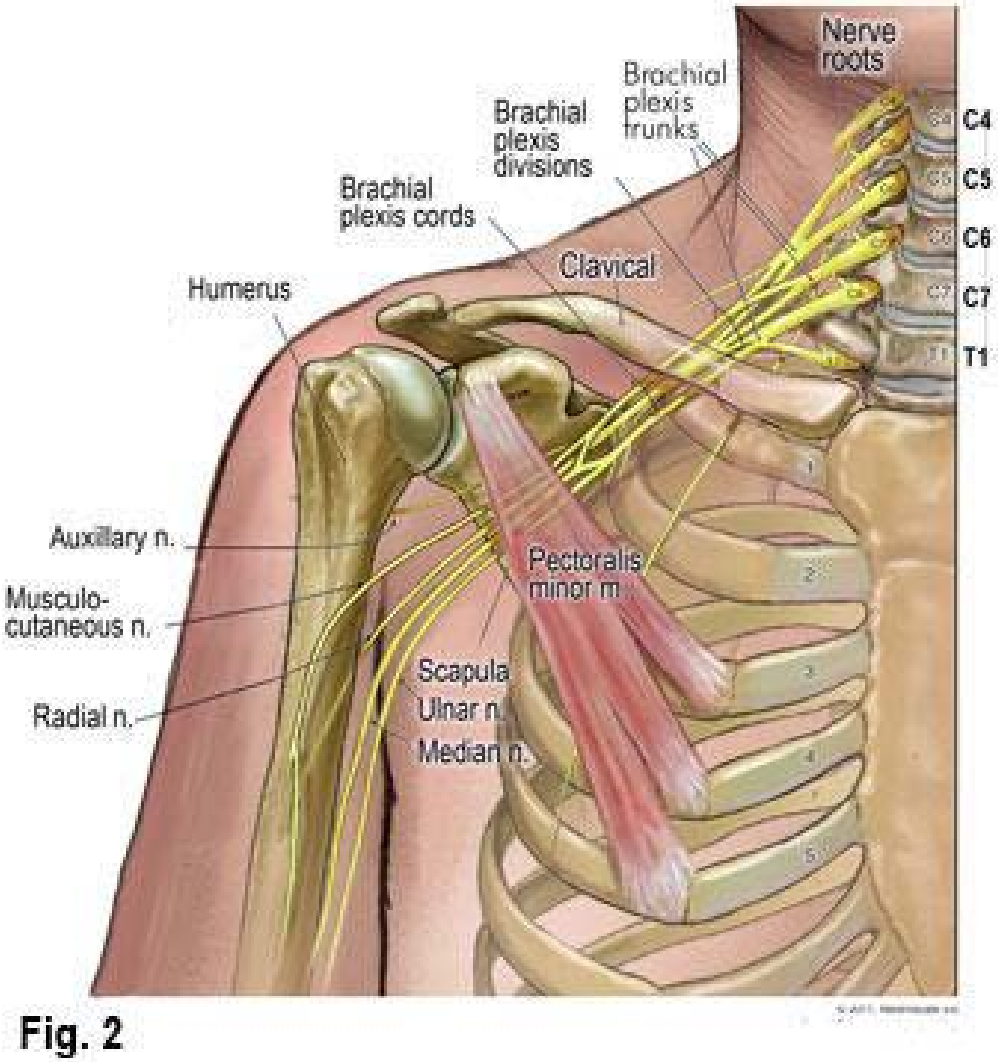


Fig. 2

FIG.1 ANATOMY OF BRACHIAL PLEXUS

Branches from the Cord:

Lateral cord:

1) Lateral pectoral Nerve (C5,C6,C7)

Motor supply- pectoralis major and minor

2) Musculocutananeous Nerve(C5,C6,C7)

Motor supply- Coracobrachialis, biceps, brachialis

Sensory supply-Lateral cutaneous nerve of arm

3) Median nerve- Lateral root (C5, C6,C7)

Medial cord:

1) Medial pectoral Nerve (C8,T1)
2) Medial cutaneous nerve of arm (C8,T1)& forearm(C8,T1)
3) Ulnar nerve (C7,C8,T1) .
    a. Motor supply-Flexor digitorum profundus, Palmaris brevis, Flexor carpi ulnaris.
    b. Sensory supply-Dorsal and palmar cutaneous branches.
    c. Deep terminal branch of ulnar nerve

        Motor supply-Flexor digiti minimi, abductor digiti minimi, opponens digiti minimi, four palmar interossei, four dorsal interossei, two lumbricals, adductor pollicis.
4) Medial root of median nerve(C8,T1)
    a. Motor supply- Pronator teres, flexor carpi radialis, flexor digitorum superficialis, Palmaris longus, lateral two lumbricals.
    b. Anterior interosseus branch: Flexor digitorum profundus, pronator quadratus, abductor pollcis brevis, flexor pollicis longus, flexor pollicis brevis, opponens pollicis.

Posterior cord:

1) Upper subscapular nerve(C5,C6)

   Motor supply- subscapularis

2) Thoraco dorsal Nerve

   Motor supply- Lattismus dorsi(C6,C7,C8)

3) Lower subscapular nerveC5, C6)

   Motor supply-subscapularis

4) Axillary nerve (C5,C6)

   a. Motor supply-Teres minor, deltoid

   b. Sensory supply- Upper lateral cutaneous nerve of arm

5) Radial nerve(C5,C6,C7,C8,T1)

   a. Motor supply- Triceps, brachioradialis, extensor carpi radialis longus.

   b. Sensory supply- Posterior cutaneous nerve of arm and forearm, lower lateral cutaneous nerve of arm.

   c. Posterior interosseous branch of radial nerve

      Motor supply- Supinator, extensors of thumb

   d. Superficial branch of radial nerve

      Sensory supply- Dorsum of hand

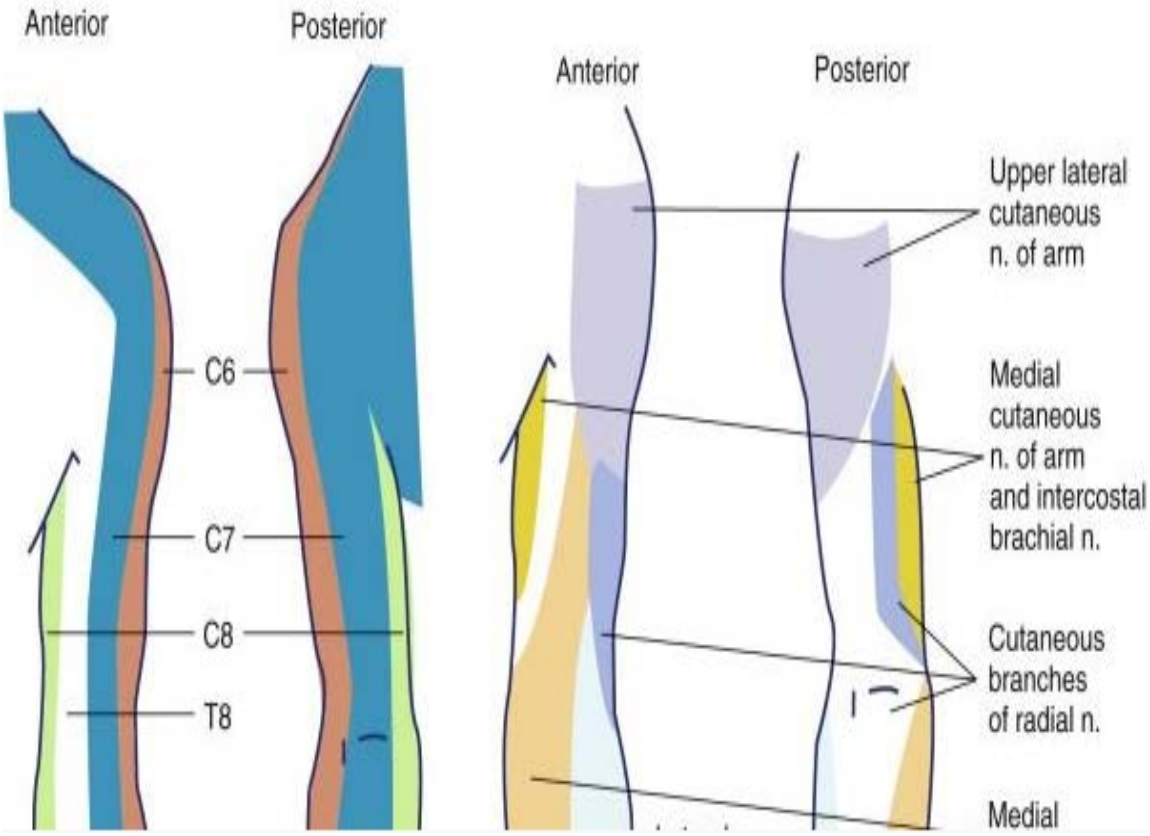


Fig 2. Cutaneous distribution of cervical plexus and peripheral nerves

ANATOMICAL LOCATION:

The plexus which is formed by the C5-C8, T1 nerve roots are coming from the corresponding intervertebral foramen and passes behind the foramen transversorium. Then it lies between the anterior and posterior tubercles of the corresponding transverse process. The five roots are situated between the anterior and medial scalene muscles. C5&C6 roots unite to form the upper trunk, C7 continues as middle trunk, C8 &T1 unite to form the lower trunk.

The trunks emerge between the two scalene muscles and passes downwards and laterally across the base of posterior triangle and then it passes across the 1st rib. At the lateral border of the 1st rib each trunk further divides into anterior and posterior division behind the clavicle. The anterior and posterior divisions unite to form the three cords.

a) Lateral cord- it is formed by the anterior divisions of the upper and middle trunks.
b) Medial cord- it is a continuation of the anterior division of the lower trunk.
c) Posterior cord - formed by all the three posterior divisions.

Sympathetic contributions of this plexus are derived from middle cervical ganglion and stellate ganglion.

Relations

ROOTS

This part of the plexus lies above the second part of the subclavian artery and between the scalene muscles.

TRUNKS

In the posterior triangle, the trunks are covered by prevertebral fascia. It is superficially placed, covered by skin, platysma and deep fascia.

Structures crossing the trunk:

Omohyoid-Inferior belly

External jugular vein

Transverse cervical artery

Supraclavicular nerves

The upper and middle trunks are situated above the subclavian artery as they pass across the first rib. The lower trunk lies behind the artery and may groove the rib immediately posterior to the subclavian groove.

DIVISIONS

At the level of lateral border of first rib and behind the clavicle, subclavius muscle, suprascapular vessels (which lies immediately posterior to the clavicle), the trunks are bifurcate into divisions and then it descends into the axilla.

CORDS:

Cords are formed at the apex of the axilla. These cords are named in relation to the axillary artery. Lateral cord- lateral to the axillary artery.Posterior cord- At first it lies lateral to the artery, when it comes behind the pectoralis minor it lies posterior to the artery. Medial cord- At

first it lies behind the artery, but when it comes behind the pectoralis minor it lies medial to the artery.

History:

- In 1880 von anrep had injected cocaine under the skin of his arm and he realised the insensitivity of that area.
- 1879&1880 –william halsted and Alfred hall injected 4%cocaine in the forearm. They found that it produces analgesia below the level of injection and not above.

  Then hall injected 2ml into the ulnar nerve at the level of elbow. It produced loss of sensation along the ulnar distribution.
- After 1893, George crile, surgically exposed the neck and injected each nerve directly.
- G.Hirschel first discovered the axillary approach.
- D.Kulenkampff first discovered the supraclavicular approach. He injected 10 ml of procaine in midclavicular area lateral to subclavian pulse.
- L.Bazy and V.Pauchet 1917-introduced infraclavicular approach
- Intravenous regional anesthesia was first introduced by August bier

SUPRACLAVICULAR BLOCK:

Indications:

- Surgery on distal upper extremity
- To palliate acute pain emergencies, herpes zoster, neuritis, upper extremity trauma, cancer
- Alternative to stellate ganglion block

Blockade level occurs at distal trunk- proximal division level.

ADVANTAGES:

- compactly arranged nerve fibres
- intensive blockade
- Small volume of drug
- Rapid onset of reliable blockade
- Can be performed with patients arm in position.

DISADVANTAGES:

- Less suitable for shoulder problems, requires cervical plexus block for supplementation
- Demonstrable paraesthesias required which is unpleasant for the patient
- 0.5 - 6% of pneumothorax incidence seen
- 40-60% phrenic nerve blockade seen

- 70-90% stellate ganglion blockade recorded
- Possibility of neuritis also seen.

Various Technique:

Classic approach : Kulenkampef

Subclavian perivascular approach : Winnes and Collins

Modified lateral paravascular approach of Moorthy

Technique

Several anatomic points are important in performance of the supraclavicular approach. The trunks are situated vertically at the level of the first rib, with the relation to the subclavian artery cephaloposteriorly, which can often be palpated in a slender, relaxed patient. At the level of the midpoint of the clavicle, the neurovascular bundle lies inferiorly. The 1st rib acts as a medial barrier to the needle reaching the pleural dome and is short, broad, and flat, with an anteroposterior orientation at the site of the plexus.

Position : supine,

Head turned to the opposite side

Arm in adducted position, hand should be extended towards the same side of the knee.

Classical technique :- Identify and mark the midpoint of the clavicle. The posterior border of the sternocleidomastoid can be palpated easily when the patient raises the head slightly. Then palpate the belly of scalenus anterior muscle, in the interscalene groove which may be situated at the level of midpoint of the clavicle around 1.5 – 2 cm posteriorly. We can palpate the subclavian pulse at this level.

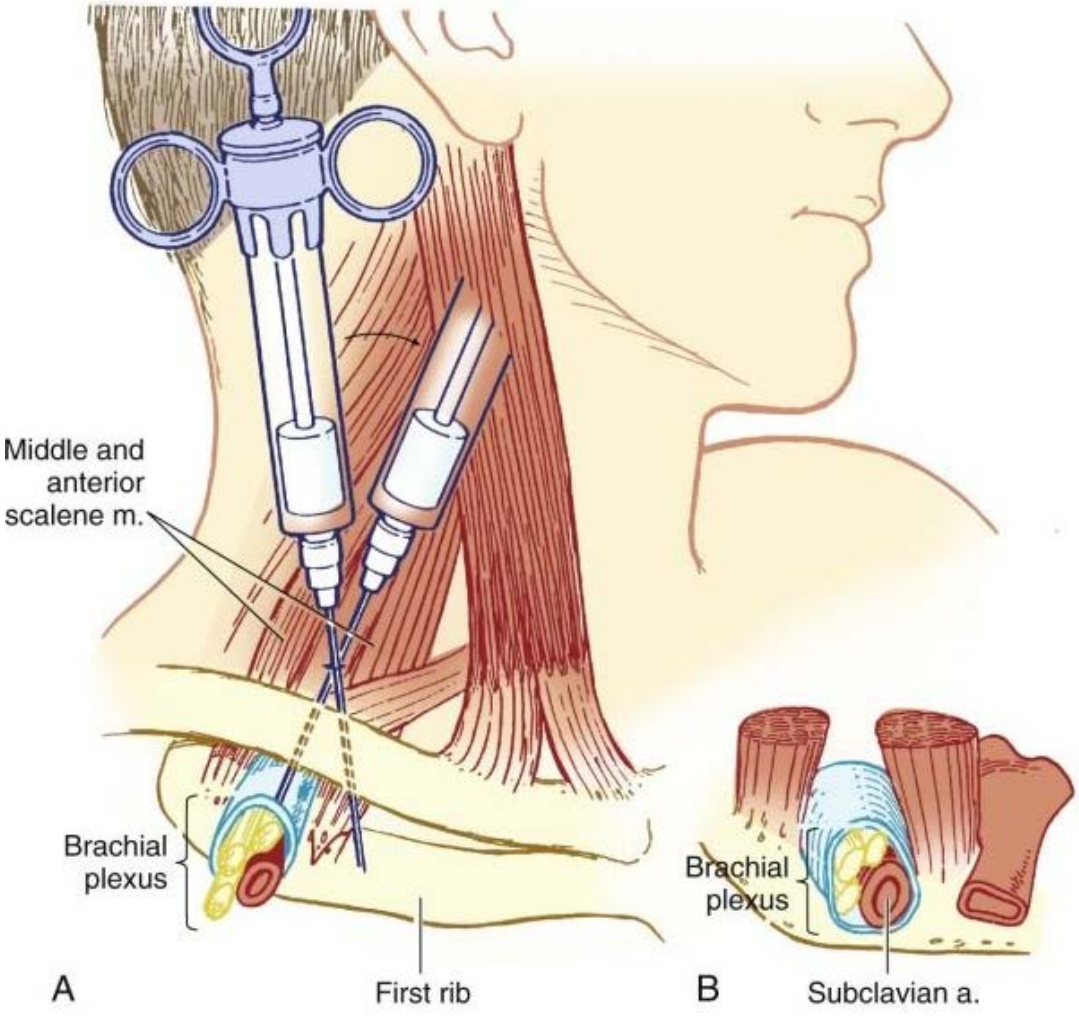


FIGURE 3 SUPRACLAVICULAR BLOCK

After appropriate preparation, a skin wheal should be created at the landmark. A 22-gauge, 4-cm needle is inserted lateral and posterior to the subclavian pulse in a caudal, medial and posterior direction until the paresthesia or motor response is elicited or the first rib is encountered. If a syringe is attached, this causes the needle and syringe to lie parallel to a line joining the skin entry site and the patient's ear. If the first rib is encountered without paresthesia, the needle should be systematically walked anteriorly and posteriorly along the first rib until the plexus or the subclavian artery is located, which results in a paresthesia or motor response. After confirming negative aspiration for blood, the local anesthetics are injected incrementally.

The rib is usually contacted at a needle depth of 3 to 4 cm. However, in an obese patient or in the presence of tissue distortion from hematoma or injection of solution, the depth may exceed the length of the needle. Nonetheless, before the needle is advanced farther, gentle probing in the anterior and posterior directions should be done at the 2- to 3-cm depth if paresthesias are not obtained. Multiple injections may improve the quality or may shorten the onset of blockade.

The modified plumb-bob approach uses similar patient positioning, although the needle entry site is at the point where the lateral border of the sternocleidomastoid muscle inserts into the clavicle. After preparation

and raising of a skin wheal, a 22-gauge, 4-cm needle is inserted while mimicking a plumb-bob suspended over the needle entry site. Frequently, a paresthesia or motor response is elicited before contacting the first rib or artery. If no paresthesia or motor response is elicited, the needle is reinserted while angling the tip of the needle cephalad and then caudad in small steps until the first rib is contacted. The modified plumb bob technique reduces the unwanted complications of classic approach[26].

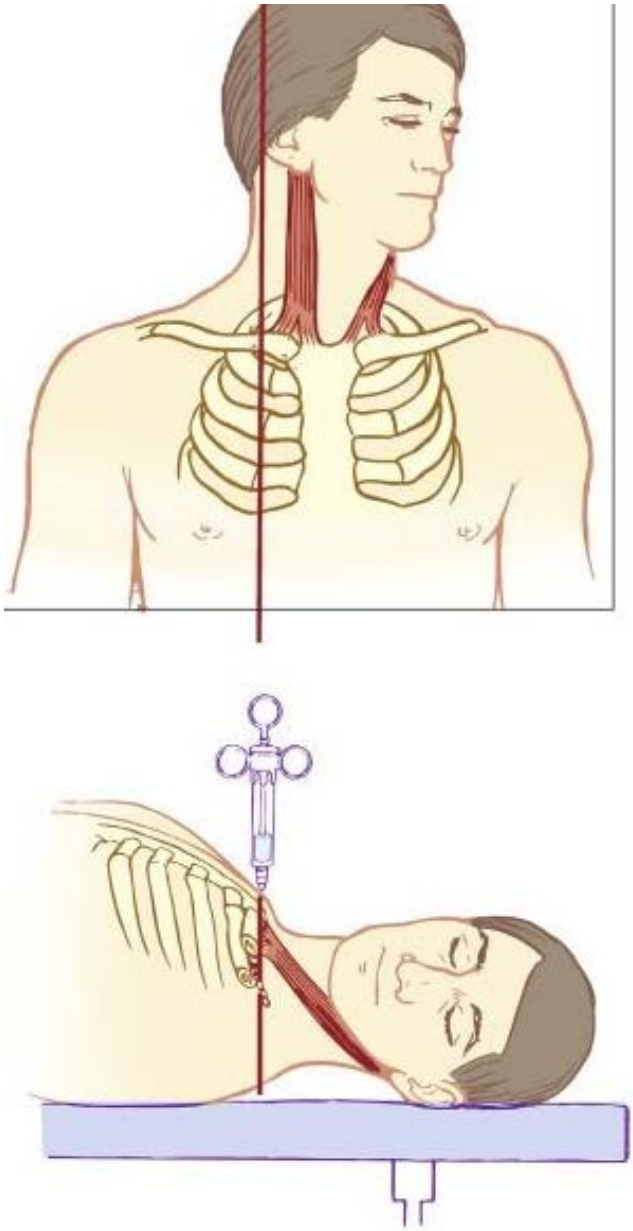


FIGURE 4 PLUMB BOB TECHNIQUE

NERVE IMAGING STUDY WITH ULTRASOUND: [25-30]

The Fascicles of peripheral nerves can be detected with a high-resolution ultrasound imaging. The fascicular echotexture is often the most distinguishing feature of nerves namely “honeycomb” architecture.

More central nerves, such as the cervical ventral rami, with fewer fascicles, therefore can appear as monofascicular on ultrasound scans.

One of the most powerful techniques to clinch the nerve fascicles is to slide a broad linear transducer on the area of peripheral target nerve.

Nerves can appear round, oval, or triangular. Although nerve shape can be changing on course, cross-sectional area is same and constant in the absence of major branching. The Peripheral nerves are pathologically enlarged also by entrapment or in certain other neuromuscular disorders such as Charcot-Marie-Tooth disease of type IA. There is also some evidence to suggest that the patients with diabetic neuropathy are also having enlarged peripheral nerves.

It is true that direct nerve imaging has led to a phenomenal good increase in ultrasound-guided regional anesthesia, but still the identification of other nearby structures like the fascia and other connective tissue is critical in this endeavor.

These significant structures permit favorable distribution of local anaesthetic that the nerve contact with the block needle is not mandated. Successful drug injections must always clarify the borders of the nerve.

ULTRASOUND AND ITS ARTIFACTS IN REGIONAL ANAESTHESIA: [31-41]

There are several common assumptions in the ultrasound imaging. First of all, the velocity of sound is assumed to be around 1540 msec. This estimate was achieved from measurements on soft tissue at physiological body temperature.

When the local heterogeneities exist, then artifactual bending of the block needle can be seen with sonography, the so-called bayonet artifact. The Speed of sound artifacts relate to the time-of-flight considerations and to the refraction at the interface of tissues with the different speeds of sound. [33,34,35]

Comet tail artifact is a type of reverberation artifact. At the low receiver gain, the comet tail is seen as a typical tapering series of discrete and clear echo bands just deep to a strongly reflecting structure.

Then spacing between the bands represents the distance seen between the anterior and posterior side walls of the object. Internal clear reverberations which arising from within the object cause the artifact of comet tail, that is most intensely observed while the object is perpendicular to the beam.

Moreover the pleura is a strong reflector that causes the comet tail artifact. Reverberation echoes are usually seen while strong specular reflections are being received.

During supraclavicular block, the mirror-image artifacts can be observed from the reverberation. While the pleura is adjacent to the subclavian artery, the mirror-image artifacts can occur with gray-scale type sonographic imaging.

Third to say, all reflectors are assumed to be on one central ray of the transducer beam. When this is not occurring true, out-of-plane artifacts are also observed that are slice thickness artifacts.

Definitive proof of the out-of-plane artifacts requires multiple views that are recommended when ambiguities arise.

Not like the adjacent tissue, biologic fluids are not significantly attenuating the sound beam and therefore will cause acoustic enhancement. The Acoustic enhancement artifacts deep to vessels may be erroneously interpreted as the nerves. For example, acoustic enhancement lying deep to the axillary artery that is in the axilla can mislead.

PHYSIOLOGY OF NERVE CONDUCTION

Autonomic postganglionic efferent and nociceptive afferent C fibres are nonmyelinated. These axons have only single Schwann cell sheath. Large motor and sensory fibres are myelinated. The myelin sheath enhances the nerve conduction and causes the action potential impulse to flow through the axoplasm to node of Ranvier. Active impulses are regenerated in nodes of Ranvier. Sodium channels are rich in nodes of Ranvier in myelinated nerve fibres. These channels are essential for impulse generation and propagation(42). In unmyelinated nerve fibers, these sodium channels are present throughout the length.

Physiology of nerve conduction:

The Nerve cells maintain a negative resting potential difference of -60 to -90mv. During rest, it is impermeable to sodium ions and permeable to potassium ions. This gradient was maintained by Na^+K^+**ATPase** (transport of three sodium ions out of the cell for two potassium ions into the cells). Permeation of these ions occur via an ion channel, a specialised protein.

Action potential:

During the stimulus, the nerve cell membrane permeable to sodium ions and changing the membrane potential to positive(43) . The threshold

for sodium ion channel opening is -55mv. During depolarisation, both sodium and potassium ion channels are in open configuration (Na>K). So excessive positive ions enter intracellularly and reversal of membrane potential to +35mv. The membrane depolarization extends to nearby the area and cause more opening of sodium channels and increasing the inward current. This event continues until some of the sodium channels became inactivated and also k^+ channels are still opened and result in a net outward current and produces repolarization. Now the threshold above the resting state, so it is refractory to next stimulus. Over time, the sodium channel inactivation decays and the potassium channel changes to closed state. Thus the resting threshold is restored.

Sodium channel has one large alpha subunit and one or two small beta subunits. Alpha subunit has four domains which is homologous DI-DIV and each has six helical regions (S1-S6) to span the membrane. It was in three states, open, inactivated and resting state.(44-45)

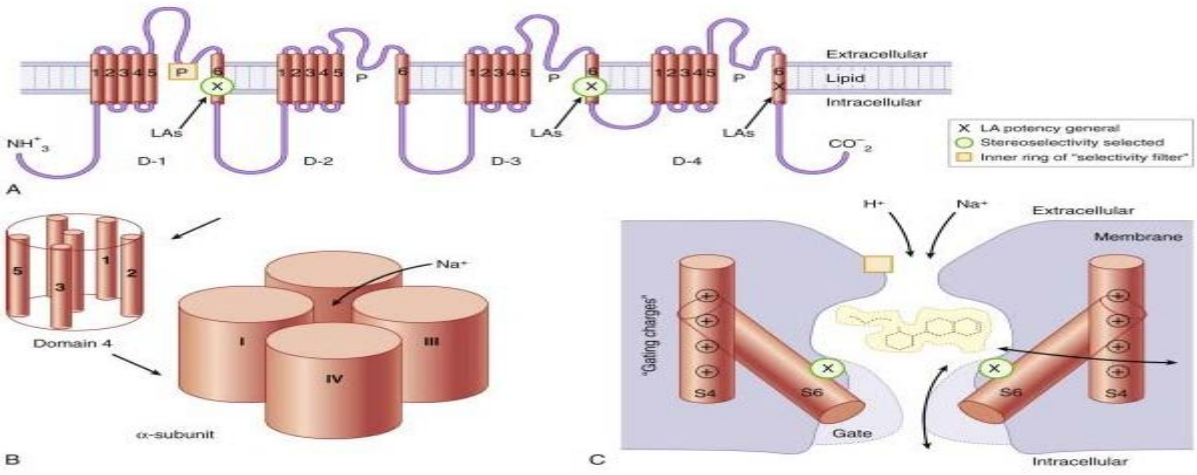


FIGURE 5 STRUCTURAL FEATURES OF SODIUM CHANNEL

LOCAL ANAESTHETICS

Local anesthetics bind with alpha subunit and block from inside of the cell (Tetrodotoxin which binds and block from outside of the cell). Local anesthetics does not alter the resting membrane potential. When increasing the concentration of local anesthetics, it slows the impulse conduction and decrease the rate of rise and magnitude of the action potential and threshold for excitation is raised progressively. Thus the propagation of impulse is abolished.

Local anesthetics have greater affinity to activated and inactivated state than the resting state. Its action is both voltage and time dependent.

Frequency dependent blockade: [46,47]

Local anesthetic action is effective, when the nerve fibres are activated rapidly. Also called as use dependent blockade or phasic block.

More depolarization causes more affinity with local anesthetics.

a) Guarded receptor model: This theory states that binding sites are more available during firing of nerve.
b) Modulated receptor model: Local anesthetics dissociates from inactivated channels slowly than from resting channels.[48]

Order of sensitivity to local anesthetics [49]

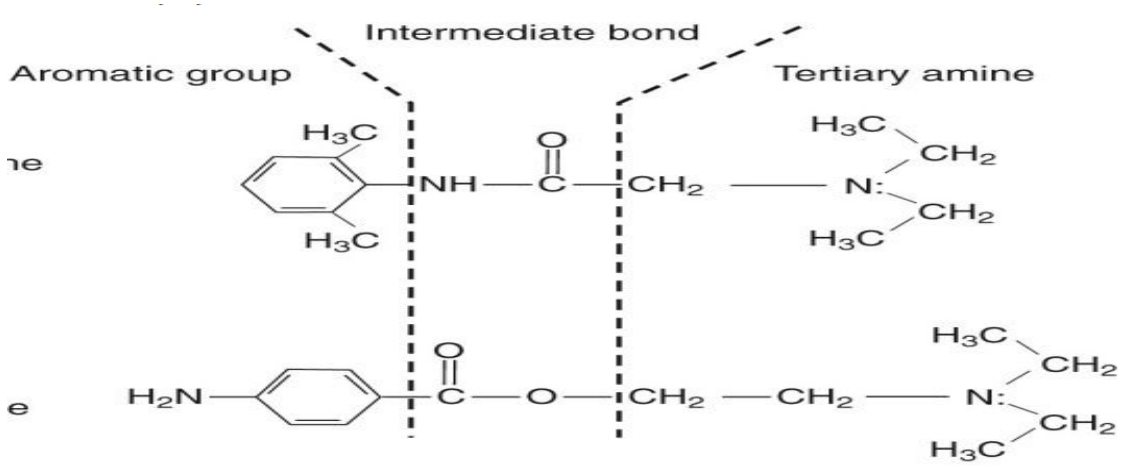
a) Small myelinated axons A γ ,Aδ
b) Large myelinated Aα, Aβ
c) Small non myelinated C fibres.

Other channels blocked by the local anaesthetics: Calcium, Potassium, NMDA

Structure of local anaesthetics:

It has three groups

1) Lipophilic – benzene ring
2) Hydrophilic end – tertiary amine
3) Intermediate chain by ester /amide



These local anesthetics are weak bases. Lipid solubility determines the potency. Local anaesthetics are poorly soluble in water, but soluble in hydrophobic organic solvents. So these drugs are prepared as water soluble hydrochloride salts with a PH of 6-7. Potency is determined mainly by lipid solubility[50].

Epinephrine is unstable in alkaline solution. So commercial preparations of local anaesthetics with adrenalin solutions are available as acidic solution(PH4-5).

Aminoester : Procaine, Chloroprocaine, Tetracaine, Cocaine

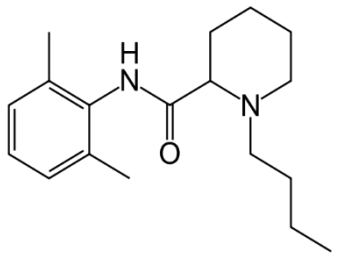
Aminoamides : Lignocaine, Bupivacaine, Ropivacaine, Mepivacaine, Prilocaine, Editocaine.

Cm- minimum concentration of local anesthetic that will block the nerve impulse conduction. Factors determining the cm are fibre size, type, myelination, PH(acidic PH antagonize the block), frequency of

nerve stimulation, electrolytes level. (hypokalemia, hypercalcemia antagonize block)[51].

Onset of action depends on lipid solubility and concentration of non ionized form. Local anesthetics with pka closest to physiological PH will have a higher concentration of non ionized base and have the fast onset property. Increasing the dose or concentration of local anesthetics cause prolonged duration of action and reduce the onset time[52,53]. But it will cause local anesthetic toxicity. Adjuvants are added with local anesthetics to avoid the side effects of local anesthetics and improve the efficacy and onset.

PHARMACOLOGY OF BUPIVACAINE



Bupivacaine is an amide type of local anaesthetic drug. It is a hydrochloride salt of 1-butyl-N-(2, 6-dimethylphenyl) piperidine-2-carboxamide.

It was synthesized in Sweden by Ekenstam and his colleagues in 1957. First used clinically by L.J. Telivuo in 1963. Pka is 8.2

Molecular weight	-	288
Protein binding	-	95%
Lipid solubility	-	28
Elimination half life	-	210mts
Toxic plasma concentration	-	>1.5µg/ml
Approximate duration of action	-	175mts

The drug is very stable to acids, alkalis and repeated autoclaving. Bupivacaine 0.5% is the preferred strength. Higher concentration result in greater variability of spread. Bupivacaine is 4 times potent than lidocaine, hence 0.5 % solution is equivalent to 2 % lidocine. It is more

cardiotoxic than lidocaine. Cardiotoxicity is aggravated by hypoxia, hypercapnia and pregnancy. It causes less motor block compared to sensory block. It is not recommended for intravenous regional analgesia. Duration of action is between 5 to 16 hours and is the longest acting local anaesthetics, which is related to binding to nerve tissue. Small percentage of a given dose of drug is excreted unchanged in the urine and the remainder is metabolized in the liver.

Uses:

- ❖ Spinal anaesthesia
- ❖ Epidural anaesthesia
- ❖ Caudal anaesthesia
- ❖ Continuous epidural anaesthesia
- ❖ Peripheral nerve block
- ❖ Infiltration anaesthesia

Onset time and duration of action

Site of action	***Onset (minutes)***	***Duration (minutes)***
Intrathecal	5	90-120
Epidural	15-20	165-225
Brachial plexus	10-20	600

Pharmacokinetics:

Once injected intrathecally, it gets absorbed by the nerve rootlets and it is rapidly absorbed from the site of injection, but the rate of absorption depends on the vascularity and the presence of vasoconstrictors. Because of high lipid solubility it easily penetrates nerve and vascular tissue. 80-95% of absorbed bupivacaine binds to the plasma proteins.

Distribution:

- Rapid distribution phase: (α)
- Slow disappearance phase: (β)

Biotransformation:

Possible pathways of metabolism of bupivacaine include aromatic hydroxylation and conjugation. Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood or urine after epidural/spinal anaesthesia. Alpha1 acid glycoprotein is the most important plasma protein binding site of bupivacaine and its concentration is increased by many clinical situations including post operative trauma.

Excretion:

4-10% of the drug is excreted in urine as unchanged form.

Mode of action

❖ Site of action:

- The spinal nerve rootlet fine nerve filaments having a large surface area are exposed to the local anaesthetics.
- Posterior and lateral aspects of the spinal cord.

❖ Sodium Channel blockade:

They impede the sodium ion access to the axon interior by occluding the transmembrane sodium channels, thus delaying the process of depolarization and the axon remains polarized. It is a non-depolarisation blockade. Thus the resting membrane potential is maintained and depolarization in response to stimulation is inhibited.

The mechanism by which local anaesthetics block sodium channel conductance is as follows,

a) Local anesthetics in the cationic form act on the receptors within the sodium channels, on the cell membrane and block it. The local anaesthetic can reach the sodium channel either via the lipophilic pathway directly across the lipid membrane or via the axoplasmic opening. This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.

b) The second mechanism of action is by membrane expansion. This is a non specific action in contrast to the more specific drug receptor interaction.

Pharmacodynamics:

It has got a longer duration of action but a slower onset.

Cardiovascular system:

Bupivacaine reduces the cardiac output by reducing the sympathetic tone, by slowing the heart rate and by reducing the venous return. It produces a fall in arterial blood pressure, but it is relatively slow and is seldom very profound. Central venous pressure is reduced. It causes an increase in lower limb blood flow, thereby it reduces the incidence of deep vein thrombosis.

Respiratory System:

It relaxes the bronchial smooth muscle. It causes apnea due to phrenic and intercostal nerve paralysis or depression of the medullary respiratory center following direct exposure to drug.

Gastro intestinal tract:

There is an increase in gastro intestinal motility and emptying of the gastric contents.

Toxicity:

Toxicity is related to the plasma level of unbound drug and more likely due to an inadvertant intravenous injection. Systemic toxicity reactions primarily involve central nervous system and cardio vascular system. The blood level required to produce central nervous system toxicity is less than that required to produce circulatory collapse.

Central Nervous System Toxicity:

The patient may have circumoral numbness, dizziness and tongue paresthesia immediately. Tinnitus and blurred vision may follow. Excitatory signs such as restlessness, agitation, nervousness, paranoia will precede central nervous system depression (slurred speech, drowsiness, unconsciousness). Muscle twitching followed by tonic clonic seizures. Respiratory arrest often follows. Selective blockade of inhibitory pathways causes these excitatory reaction.

Cardiovascular System Toxicity(54-56)

The rate of depolarization in fast conducting tissue of purkinje fibres and ventricular muscle is decreased. The rate of recovery of bupivacaine induced block is slower than that of lignocaine. Extremely high concentration of the drug causes sinus bradycardia, hypotension, atrioventricular heart block, idioventricular rhythms and life threatening arrhythmias such as ventricular tachycardia, ventricular fibrillation and

cardiac arrest. Levobupivacaine S(-) isomer is devoid of some of the CNS and CVS adverse effects. It will prevent the toxic effects following inadvertent intravascular injection of bupivacaine.

The dosage of bupivacaine depends on,

- Area to be anaesthetized
- The vascularity of the tissue to be blocked
- The number of neuronal segments to be blocked
- Individual tolerance
- Technique of local anaesthesia.

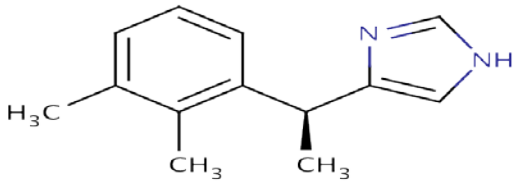
Available concentrations:

- 0.25%,0.5%
- 0.25%,0.5% soluble in isotonic saline
- 0.5% 0.75% solution in 8% dextrose hyperbaric
- These doses can be repeated in 3-4 hours but maximum dose is 400mg in 24 hours.

Dosage and concentration of bupivacaine in various blocks

Type of block	Concentration	Dosage in ml	Dosage in mg
Local infiltration	0.25-0.5%	5-20ml	Upto 75 mg
Brachial plexus block	0.25-0.5%	20-40ml	75-225 mg
Intercostal block	0.25-0.5%	3-5ml	15-20mg per each nerve
Epidural block	0.25-0.5%	15-20ml	50-200mg
Caudal block	0.25-0.5%	15-30ml	75-150mg
Subarachnoid block	0.5%	2-4 ml	10-20mg

PHARMACOLOGY OF DEXMEDETOMIDINE



Dexmedetomidine is an $\propto_2$- agonist that received FDA approval in 1999. It is used as a short-term sedative analgesic especially in the ICU and usually not used for more than 24 hours[57]. Dexmedetomidine is a selective $\propto_2$ – adrenoceptor agonist. It is used in high doses for sedation and analgesia. It has a reversal drug Atipamezole for its sedative effect. It is used in perioperative period as sedative and analgesic, as premedication, as an anesthesic adjunct for general as well as regional anesthesia and also for post operative sedative and analgesic.

Physiology of $\propto_2$ -adrenoceptors.

Alpha 2 – adrenoceptors are found in peripheral and central nervous systems, also in effector organs like liver, kidney, pancreas, eye, vascular smooth muscles and platelets.

They are divided into 3 subtypes.

- ★ $\propto_2$ A- predominant subtypes in CNS, this is responsible for the sedative, analgesic and sympatholytic effect. Dexmedetomidine is 8 to 10 times more selective towards $\propto_2$ AR than Clonidine.
- ★ $\propto_2$ B –found mainly in the peripheral vasculature, and is responsible for the short term hypertensive response.
- ★ $\propto_2$ C-found in the CNS, which is responsible for the anxiolytic effect(58) ,startle response.

Startle response is the response of mind and body to a sudden unexpected stimulus, such as flash of light, loud noise. In human beings, the reaction includes physical movement away from the stimulus, the contraction of the muscles of arms and legs,blinking , respiratory and blood pressure changes.

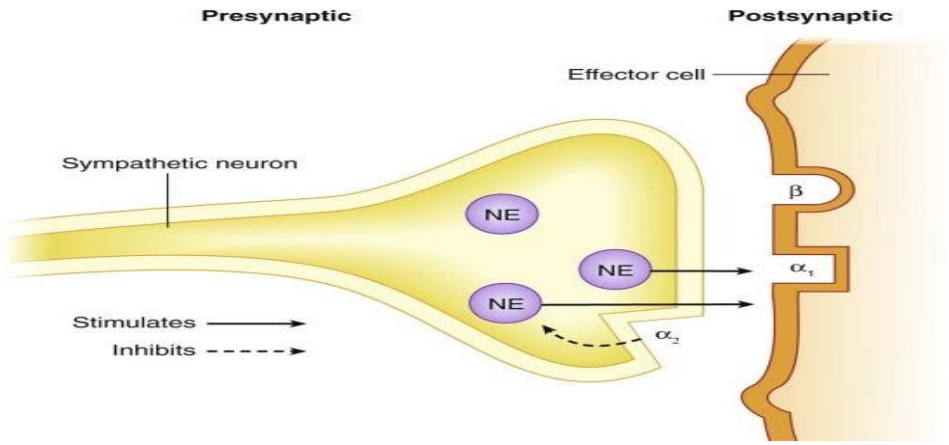


Fig 6 preganglionic and postganglionic alpha receptors of sympathetic nervous system

All these subtypes produce cellular action by signalling through a G-Protein which couples to effector mechanisms, and the coupling differs depending on receptor sub-type and location. The $\propto_2$ A-Subtype appears to couple in an inhibitory fashion to the calcium channel in the locus ceruleus of the brain stem and in the vasculature. The $\propto_2$ B subtype couple in an excitatory manner to the same effector mechanism.

Mechanism of action of dexmedetomidine:

Dexmedetomidine possess unique properties and it differs from other sedative drugs. $\propto_2$ – adrenoceptors are found in many sites throughout the CNS, but the highest densities are found in the locus ceruleus, the predominant noradrenergic nuclei of the brainstem which is an important modulator of vigilance(59). Presynaptic activation of $\propto_2$ adrenoceptor in the locus ceruleus inhibits nor epinephrine (NE) release and results in sedative and hypnotic effects. Locus ceruleus is the site of origin for descending medullospinal noradrenergic pathway which is an important modulator of nociceptive neuro transmission. Stimulation of the $\propto_2$ –adrenoceptors in this area terminates mainly the propagation of pain signals leading to analgesia. Post synaptic activation of $\propto_2$ – adrenoceptors in the CNS causes decrease in sympathetic activity which leads to hypotension and bradycardia. Also cardiac vagal activity is

augmented and all the effects together produce analgesia, sedation and anxiolysis.

Stimulation of $\propto_2$ –receptors at the substantia gelatinosa causes inhibition of the nociceptive neurons firing and inhibition of substance P release.$\propto_2$adrenoceptors also have analgesic mechanisms by inhibiting norepinephrine release at the nerve endings whereas the reason for analgesic effect is by the spinal mechanism.

$\propto_2$ - Receptors located on blood vessels which mediates vasoconstriction whereas those located on sympathetic terminals inhibit norepinephrine release. In other areas these $\propto_2$ adrenoceptors cause contraction of vascular and other smooth muscles, decreased salivation, secretion and bowel motility in the gastrointestinal tract. It also inhibit the release of renin , increased glomerular filtration rate, decreased insulin release from pancreas, decreased intraocular pressure, decreased platelet aggregation and decreased shivering threshold by 2^oC.[60]

Pharmacokinetics:

Absorption and distribution:

Dexmedetomidine with the dose of 0.2 to 0.7 µg/kg /hr exhibits linear pharmacokinetics and it is administered as intravenous infusion

upto 24 hours. Also it has the rapid distribution phase, its distribution half life is around 6 minutes [61], and elimination half life is 2 hours.

The volume of distribution is 118L. Average protein binding is 94%. Context- sensitive half life ranges from 4 minutes after a 10-minute infusion to 250 minutes after an 8-hour infusion. Its oral bioavailability is poor, which is because of extensive first-pass metabolism. The bioavailability of sublingual route is high (84%) and it offers a potential role in pediatric sedation and premedication.

Metabolism and excretion

Dexmedetomidine undergoes biotransformation through direct N-glucuronidation and cytochrome P-450 (CYP 2A6) mediated aliphatic hydroxylation to its inactive metabolites. Metabolites are excreted in the urine(95%) and in the feces (4%). Dose has to be reduced in patients with hepatic failure.

Pharmacodynamics

∝- adrenoceptor agonists have different $\propto_2$ / $\propto_1$ selectivity.$\propto_2$ / $\propto_1$ selectivity of dexmedetomidine is 1620:1 whereas it is low for clonidine and hence dexmedetomidine is 8 times more powerful $\propto_2$ – adrenoceptor than clonidine.

Cardiovascular system

Dexmedetomidine has no effects on the heart directly. It causes a dose dependent increase in coronary vascular resistance and oxygen extraction and the supply / demand ratio is unaltered. It evokes a biphasic blood pressure response. A short hypertensive phase and subsequent hypotension and the 2 phases are mediated by 2 different $\propto_2$ –AR Subtypes: the ∝-2B AR is responsible for the initial hypertensive phase. Hypotension is mediated by the ∝2A –AR.(62) Younger patients with high level of vagal tone develop bradycardia and sinus arrest which were effectively treated with anticholinergic agent.

Respiratory system

Dexmedetomidine does not produce respiratory depression even at high doses (63). It can be safely used in spontaneously breathing patients after surgery in ICU. It maintains sedation without cardiovascular instability or respiratory drive depression. Hence it is used during weaning and extubation in trauma / surgical ICU Patients in whom previous attempts at weaning have failed because of agitation associated with hyperdynamic cardio pulmonary response [(64).]

Central nervous system

Dexmedetomidine reduces cerebral blood flow and cerebral metabolic requirement of oxygen. Dexmedetomidine enhances cumulative performance and also possess sedative, analgesic and anxiolytic action through $\propto_2$–AR(65) .It reduces levels of circulating and brain cetecholamines, thus balancing the ratio between cerebral oxygen supply and demand, reduces excitotoxicity and improves the perfusion in the ischemic penumbra, hence it possess excellent neuroprotective action. In subarachnoid haemorrhage it reduces the levels of glutamate which is responsible for cellular brain injury.

Endocrine and renal effects

Dexmedetomidine activates peripheral presynaptic $\propto_2$–AR, thus catecholamine release is reduced and hence sympathetic response to surgery is also reduced. It is an imidazole agent but does not inhibit steroidogenesis when used as an infusion for short term sedation[(66).]

Adverse Effects:

Side effects reported are hypotension, hypertension, nausea, vomiting, dry mouth, bradycardia, atrial fibrillation, pyrexia, chills, pleural effusion, atelectasis, pulmonary edema, hyperglycemia, hypocalcaemia, acidosis, etc., Transient hypertension is produced when dexmedetomidine infusion is rapidly administered (Loading dose of

1µg/Kg / hr if given less than 10 minutes) and this is mediated by peripheral ∝2B –AR vasoconstriction[67].

The occurrence of Hypotension and bradycardia is mediated by central ∝2A-AR, causing decrease in noradrenaline release from the sympathetic nervous system. Supersensitization and up regulation of receptors occur during long term use, hence abrupt discontinuation not advised. Withdrawal symptoms of nervousness, agitation, headache and hypertensive crisis occur during abrupt discontinuation.

Clinical applications of dexmedetomidine premedication

Dexmedetomidine is used as an adjuvant for premedication since this drug possess sedative, anxiolytic, analgesic, sympatholytic, and stable homodynamic profile. Premedication dose is 0.33 to 0.67 mg /kg IV given 15 minutes before surgery. Oxygen consumption is decreased in intraoperative period and in post operative period [68].

Intra operative use:

Dexmedetomidine attenuates the homodynamic stress response which occurs during intubation and extubation by sympatholysis[69]. Dexmedetomidine potentiates anesthesic effect of all the anesthesic agents, thus reducing their requirement [70].

Regional anaesthesia

Highly lipophilic nature of dexmedetomidine facilitates rapid absorption into the cerebrospinal fluid. It binds to $\propto_2$ – AR of spinal cord for its analgesic action[79]. Sensory and motor block produced by local anesthetics is prolonged. It is also used in intravenous regional anaesthesia (IVRA), brachial plexus block and intraarticularly. It is also given through intraarticular route in arthroscopic knee surgeries to improve the duration of postoperative analgesia[71].

Sedation in ICU

Dexmedetomidine produces cooperative sedation. It does not interfere with the respiratory drive hence it facilitates early weaning from ventilator, thus reducing ICU stay and costs [72]. Many studies have recommended their use for longer than 24 hrs. Their other beneficial effects are minimal respiratory depression, analgesic sparing effects, reduced delirium and agitation, and desirable cardio vascular effects.

Procedural sedation

Dexmedetomidine is used for short term procedural sedation like transesophageal echocardiography[73], colonoscopy[74], awake carotid endarterectomy[75], shockwave lithotripsy[76], elective awake fiberoptic intubation [77],pediatric MRI(78). The dose is 1 µg/kg with a maintainance dose of 0.2µg/kg/h.

Controlled hypotension(80-81)

Spinal fusion surgery for idiopathic scoliosis, septoplasty and tympanoplastyoperations and maxillofacial surgery have been done with dexmedetomidine induced hypotension.

Analgesia

Dexmedetomidine activates ∝2 –AR in the spinal cord, thus the transmission of nociceptive signals is reduced. It possesses significant opioid sparing effect.

Cardiac surgery(82)

Dexmedetomidine reduces the extent of myocardial ischemia during cardiac surgery.

Neurosurgery(83)

Dexmedetomidine possess neuro protective effect. It also attenuates delirium and agitation, so that postoperative neurological evaluation will be easier. It has a role in functional neurosurgery like awake craniotomy surgeries and implantation of deep brain stimulators for Parkinson’s disease.

Obesity

In morbidly obese patients this drug does not cause respiratory depression in the dose of 0.7µg /kg intra operatively.

Obstetrics(84)

Dexmedetomidine is also used in obstetrics due to its maternal hemodynamic stabilizing property. It also produces anxiolysis and stimulation of uterine contractions. Since it is highly lipophilic it does not cross placenta and hence it causes less chance of fetal bradycardia.

Pediatrics

Recently it is used in pediatric patients for sedation during non-invasive procedures in radiology like CT scan and MRI[(85)].

Other uses

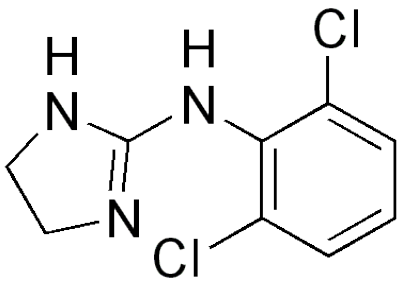
a) Used as an anti-shivering agent
b) Used as an alternative to clonidine unresponsive patient
c) Used in the treatment of withdrawal from benzodiazepines, opioids and alcohol.

CLONIDINE

History and chemistry(86-90)

Clonidine hydrochloride, an imidazoline derivative was introduced as a nasal decongestant and vasoconstrictor. This drug is related to the drug called naphazoline, still this has complex profile of actions. Its hypotensive and bradycardia effects were first appreciated in 1962. It is a centrally acting adrenergic agonist that lowers blood pressure by decreasing basal sympathetic system activity. it was introduced in Europe in1966 and subsequently in the U.S as an antihypertensive agent.(220:1 alpha2:alpha1).

Structure



2-(2,6_-dichlorophenylamino)-2 – imidazoline hydrochloride.;

C9H9C12N3 Hcl. Molecular weight :266.56.

It is an odorless, white, bitter crystalline substance soluble in alcohol and water.

Mechanism of action

Alpha-2 adrenergic agonists produce clinical effects by binding to alpha-2 receptors. It is a centrally acting partial adrenergic agonist (alpha2:alpha1=220:1). Alpha 2 receptors densely found in pontine locus ceruleus which is an important source of sympathetic nervous system innervations of the forebrain and a vital modulator of vigilance. The sedative effect is inhibition of this nucleus. It also stimulates alpha 2 adrenergic inhibitory neurons in the medullary vasomotor centre. All these leads to decreased sympathetic nervous system outflow from the central nervous system to peripheral tissues and manifested as peripheral vasodilatation and a decrease in systolic blood pressure, heart rate and cardiac output. Clonidine has the ability to modify the potassium channels in the CNS and hyperpolarize the membranes. So it reduces the anesthetic requirements.

Neuraxial placement of clonidine inhibits substance P release and nociceptive neuron firing produced by the noxious stimulation. Alpha 2 afferent terminals are situated centrally and peripherally, in the superficial laminae of the spinal cord and several brainstem nuclei. This suggests the analgesic effects of clonidine are more pronounced after neuraxial administration. Clonidine synchronously decreases the cold response threshold while slightly increasing the sweating threshold thus suggesting

that it acts on the central thermoregulatory system rather than preventing shivering peripherally.

Pharmacological effects:

Intravenous clonidine can cause a transient rise followed by a fall in blood pressure due to its peripheral vasoconstrictive effect on alpha 2 receptor on vascular smooth muscle of skin and mucosa and decrease in BP is due to central effect by reduction of sympathetic outflow from CNS and reduction in the release of nor epinephrine at the nerve terminals .

Pharmacokinetics:

Clonidine is rapidly absorbed after oral intake and 100% bioavailable. Within 60 to 90 minutes it will reach the peak plasma concentration. The elimination half life is around 9-12 hours.50% is metabolized in the liver and 50% is excreted in an unchanged form by the kidney. Its half life is increased in renal failure and liver failure. A transdermal delivery system is available in which the drug is released at a constant rate for about a week. Three to four days are required to achieve steady state concentrations.

Side effects :

The most common is sedation and xerostomia. Fatigue, weakness, headache, withdrawal syndrome. Pallor, weakly positive coombs test and fever may also rarely occur.

Cardiovascular system :

Orthostatic symptoms, palpitation, tachycardia, bradycardia, conduction abnormalities (i.e, junctional bradycardia, high degree Atrioventricular block and sinus node arrest) congestive heart failure, raynauds phenomenon and syncope.

Central nervous system :

Nervousness, mental depression, insomnia, agitation, may occur. Other behavioral changes, vivid dreams or nightmares, hallucinations and delirium are rarely reported.

Dermatological : Rash, pruritis,angioneurotic edema and urticaria, alopecia.

Gastrointestinal : Nausea, vomiting,anorexia,malaise, abnormalities in LFT constipation and abdominal pain rarely.

Genitourinary : Decreased sexual activity, impotence,

Hematological : Reduced platelet count rarely.

Metabolic : Weight gain, gynecomastia, transient hyperglycemia[91], increased serum CPK

Musculoskeletal : Myalgia, arthralgia, leg cramps.

Interactions with various other pharmacological preparations :

This drug may also like other ones are seen to be reacting with other drugs namely:

- Tricyclic anti-depressant drug
- Chlorpromazine

Because of these specific interactions, the intended anti-hypertensive nature of the drug may be very much reduced and affected. Clonidine can cause bradycadia or AV block. So it should be used with caution in patients who are on digitalis, calcium channel blockers,beta blockers.

Toxicology;

Some of the studies supported the occurence of spontaneous retinal degeneration in albino rats treated with clonidine for more than six months. In some studies conducted in dogs and monkeys clonidine showed a high drug concentration in choroid .But in human studies they documented dryness of eyes only. In electroretinography ,macular dazzle retinal function was normal.

Over dosage;

Hypertension followed by fall in blood pressure, heart rate, respiratory rate, temperature, altered consciousness, decreased or absent

reflexes, seizures, weakness and miosis. Reversible cardiac conduction abnormality, apnea, coma may occur. Toxic effects are developed within 30 minutes to two hours after exposure. In paediatric patients, even a small dose of 0.1mg clonidine may produce toxic effects.

Antidote:

There is no specific antidote for clonidine. In recently ingested patients, gastric lavage, activated charcoal may be useful. Supportive care may include anticholinergic for bradycardia, IVF and vasopressors for hypotension and vasodilators for hypertension. Naloxone may useful for clonidine induced respiratory depression,hypotension coma . Dialysis is not much useful.

Available forms:

Formulations	**Brand**	**Dosage**
Oral tablets	Clonidine tablets	0.1,0.2,0.3mg
Transdermal patch	Clonidine TTS	0.1,0.2,0.3g 3mg/day
Combination tablets	Clonidine and Chlorthalidone	0.1,0.2 or 0.3 mg clonidine+15mg chlorthalidone
Injection	Cloneon, duraclon	500,150,100mcg/ml

Various routes of clonidine

Route	Dose
Intranasal	2-4mcg/kg
Intramuscular	2mcg/kg
Oral	4-5mcg/kg
Rectal	2.5-5mcg/kg with atropine 40mcg/kg
Intravenous	1-2mcg/kg bolus or 0.18-3.16 mcg/kg/hr infusion
Caudal anaesthetic adjuvant	1-2mcg/kg
Spinal anaesthetic adjuvant	1-2mcg/kg
Epidural anaesthetic adjuvant	0.0625%bupivacaine with fentanyl 1mcg/ml and clonidine 0.6 mcg/ml
Sciatic block	0.2% ropivacaine 0.4mg/kg/hr with clonidine 0.12 mcg/kg/hr infusion

Anesthetic uses of clonidine

The anesthetic use of an alpha 2 adrenergic receptor agonist has been of recent research interest over last 20 years.

Premedication

It reduces anaesthetic dose requirements and MAC of volatile anaesthetics. It can be used as premedication. In addition it also has an anaesthesia sparing effect. Clonidine is recommended in doses of 4mcg/kg intranasally or orally and rectally in a dose of 5mcg/kg causes

adequate sedation. Routine use of anticholinergic with clonidine reduces the incidence of bradycardia and hypotension.

However we have to reduce the doses of IV induction agents when clonidine is used as premedicant. Otherwise patient may have hypotension and bradycardia after induction during anesthesia.

Its use as a premedicant is more useful in certain group of patients like [96,97]

- Drug addicts and alcoholics. Most of these patients have withdrawal symptoms and their sympathetic system activity is high when compared to normal patients.
- Patients on chronic opioid or analgesic treatment for cancer pain. These patients have increased analgesic requirement intraoperatively.[92]
- Hypertensive patients who are vulnerable to blood pressure swings.

Control of hemodynamic response:

The hemodynamic effects of clonidine are both central and peripheral. Stimulation of the peripheral sub endothelial receptor causes vasoconstriction transiently.

Stimulation of alpha 2 adrenergic receptors of the neurons in the nucleus tractus solitarius causes inhibition of nucleus of sympathetic

neurons in the medulla, and reduces the baroreflex activity, decreases the atrial pressure leading to fall in heart rate. It is interesting to note that phasic activity of this reflex is preserved. So that any decrease in arterial pressure is followed by a significant increase in heart rate. It depresses the presynaptic sympathetic neurons at thoracic spinal cord level (lateral horn). Local administration of neostigmine inhibits this effect. Hypotension effect is more in intrathecal than intravenous route. Vasoconstrictors (eg.phenylephrine) and anticholinergics are used to treat the hypotension and bradycardia.

Clonidine prevents stress response to laryngoscopy, intubation, extubation and surgical stimulation. It inhibits shivering. Patients undergoing cardiac surgery and vascular surgery have superior control of hemodynamics, reduces the incidence of myocardial ischemia and decrease the morbidty and mortality.

Post operative analgesia and regional anesthesia: [93]

It inhibits transmission of nociceptive stimuli in the dorsal horn of the spinal cord. Clonidine has additive effect with opioids and augment local anesthetic blockade and prolongs the duration of anaesthesia.

Epidural:

It can be used as whole anesthetic agent to produce epidural analgesia in large dose (upto2-3000mcg/day). At this dose hypotension, bradycardia is common. It is more commonly used along with local anesthetics and opioids at a dose of 10-15 mcg/hr.

Spinal:

Compared to morphine, intrathecal clonidine produces analgesia of shorter duration but without respiratory depression or urinary retention, 1-2mcg/kg can be given along with local anaesthetics.[94,95]

Caudal:

Clonidine prolongs duration of the block without hemodynamic alterations. The recommended dose is 1-2mcg/kg.

Labor analgesia:

Epidural clonidine can be used alone or with opioids or local anaesthetics. Clonidine crosses the placenta but does not affect the newborn. The recommended dose is 100mcg during labor.

Peripheral nerve blockade:

Clonidine reduces the failure rate, reduces the local anaesthetic dose requirement and prolongs the duration of post operative analgesia. A

small dose of 2-3mcg/kg is sufficient which obviously reduces the risk of side effects.

The quality of bier's block (IVRA) by clonidine with lignocaine is improved. Addition of 150mcg clonidine has been found to enhance the tolerance of the tournique.

Other uses are

* Prevention of emergence agitation
* Decreasing minimum alveolar concentration of sevoflurane
* Studies have found that oral clonidine 4mcg/kg given 105 minutes before induction decreased MAC values of sevoflurane for LMA insertion.
* Postoperative nausea and vomiting (PONV).

Hypotensive anesthesia

In cardiovascular surgery; better hemodynamic stability in patients posted for cardiac surgery.

Post operative shivering :

Clonidine is effective in treating postoperative shivering in children. 1.5 mcg/kg is required to stop shivering in 5 minutes.

Day care surgery :

Oral clonidine premedication and new safer local anesthetics ropivacaine or levobupivacaine with clonidine adjuvants as single caudal shots prolong analgesia with minimal side effects.

Contraindication:

Clonidine is contraindicated in

* Hypovolemia
* A-Vblock
* Prolonged PR interval
* Sinus bradycardia

MATERIALS AND METHODS

STUDY DESIGN

Prospective randomized comparative double blinded study

POPULATION

6O patients

INCLUSION CRITERIA

- ASA I, II
- Age 20 to 50
- Unilateral upper limb orthopaedic surgeries
- Both sexes

EXCLUSION CRITERIA

- Patient Refusal
- Patients on adrenoreceptor agonist or antagonist therapy.
- Suspected coagulopathy
- Infection at the site of block
- History of respiratory, cardiac, hepatic or renal failure.
- Patients with medical complications like severe anemia, severe hypovolemia, shock, septicemia.
- Allergy to local anaesthetics and study drug.
- Pregnant women.

SAMPLE SIZE

- Group BC (N = 30) – 35 ml of 0.357%bupivacaine + 2mcg/kg clonidine.
- Group BD (N = 30) – 35 ml of 0.357% bupivacaine + 2mcg/kg dexmedetomidine.

PRE OPERATIVE EVALUATION

In all the patients,

- Age
- I.P. No
- Body weight and
- Baseline vital parameters were recorded.

History regarding previous anaesthesia, surgery, any significant medical illness, medications and allergies were recorded. Complete physical examination and airway assessment were done. Following laboratory investigations were done:

- Haemoglobin %,
- Blood sugar & urea
- Serum creatinine
- Urine analysis.
- Chest x ray , ECG

- ❖ Bleeding time and clotting time
- ❖ Screening for HIV, HbsAg

STUDY METHOD

After getting approval from the institutional ethical committee, informed written consent were obtained from the patients. The patients were randomly allocated into two groups according to computer generated random numbers. Preliminaries:

a) For the procedure:

- A portable tray covered with sterile towels containing:
- Sterile syringes –two twenty ml syringe
- Hypodermic needles of 5 cm length,22G
- Povidone iodine and spirit
- Sponge holding forceps
- Towels and towel clips
- Sterile gauze pieces

b) For emergency resuscitation:

- The anaesthesia machine,emergency oxygen source (E type cylinders), pipeline 02 supply, working laryngoscopes, appropriate size ET tubes
- Working suction apparatus

- Oropharngeal airway
- Intravenous fluids.
- Drugs : thiopentone, diazepam, succinylcholine, hydrocortisone, atropine, adrenalin, aminophylline, mephenteramine, calcium gluconate and sodium bicarbonate.

c)Monitors:

- Pulse oximeter.
- Non invasive blood pressure monitor by sphygmomanometer on the opposite limb.

Patients were premedicated with inj.atropine 0.02mg/kg i.m 45 minutes before surgery. After insertion of a 18-gauge intravenous cannula in the contralateral arm, Ringer Lactate fluid was started. Standard monitoring was used during anaesthesia and surgery. HR, MAP and SpO2 were recorded before surgery and at regular intervals during and after the surgery. Procedure : patient lies supine, arms by the side and head turned slightly to the opposite side.

* Identify the interscalene groove and mark the midpoint of clavicle.
* with aseptic preparation , a point of around 1.5 to 2.0 cm cephalad and posterior to midpoint of clavicle, the subclavian

pulse was felt. A skin wheel was raised with local anaesthetic just cephalo-posterior to the pulsations.

* Next ,a 22 gauge ,5cm needle ,mounted on a 20ml syringe,was passed through the same point,parallel to the head and neck,caudally and medially and posteriorly ,until the paresthesia was elicited or 1 st rib was encountered.
* If the 1st rib was encountered, the needle would be walked over the first rib until a paresthesia was elicited either in the arm or hand
* After conforming the negative aspiration of blood, drugs were injected by the observer who was blind to the patient group.
* All patient were monitored for anaesthesia and analgesia upto 16 hours post operatively.

Sensory block was assessed by sensations to pinprick on skin dermatomes C4toT2. Whereas motor blockade was assessed by movements in the thumb:

- Adduction for ulnar nerve,
- Abduction for radial nerve,
- Opposition for median nerve,
- Flexion of elbow, the supination and the pronation of forearm for musculocutaneous nerve were assessed.

Intraoperative and post operative complications were also noted and recorded to know the outcome of the study.

Hollmen scale was used to examine sensory as well as motor block.

HOLLMEN SCALE:

FOR MOTOR BLOCK:

- Normal level of function of muscle = 1
- Mild level function weakness = 2
- Moderate level function weakness =3
- Total action of muscle lost = 4

Sensory block assessment:

- Good level pinprick sensation = 1
- Pointed sharp weak sensation than other hand = 2
- Perceived sense- blunt touch with needle=3
- Nil sensation to pinprick =4

Examination was conducted every one minute after giving the drug and the time taken for initiation of the motor and sensory block was noted. Time for onset is explained as level of at least grade 2 in measuring hollmen's scale.

Time for complete block is defined as when motor, sensory scores amount to grade 3 according to hollmen scale. Total time of motor block is explained to be the time from the injection of the drug and recovery of muscle power.

Total duration of sensory block is defined as the time from giving the drug and the time when patient complaints pain in the post operative period.

STATISTICAL ANALYSIS

Software Name : SPSS 20 and Sigma Stat 3.5 versions

Tests used:

- One way ANOVA,
- Student's test,
- Pearson Correlation for Datas
- Chi square test for consolidated figure.
- p‟ value of < 0.05 taken as significant.

OBSERVATION AND RESULTS

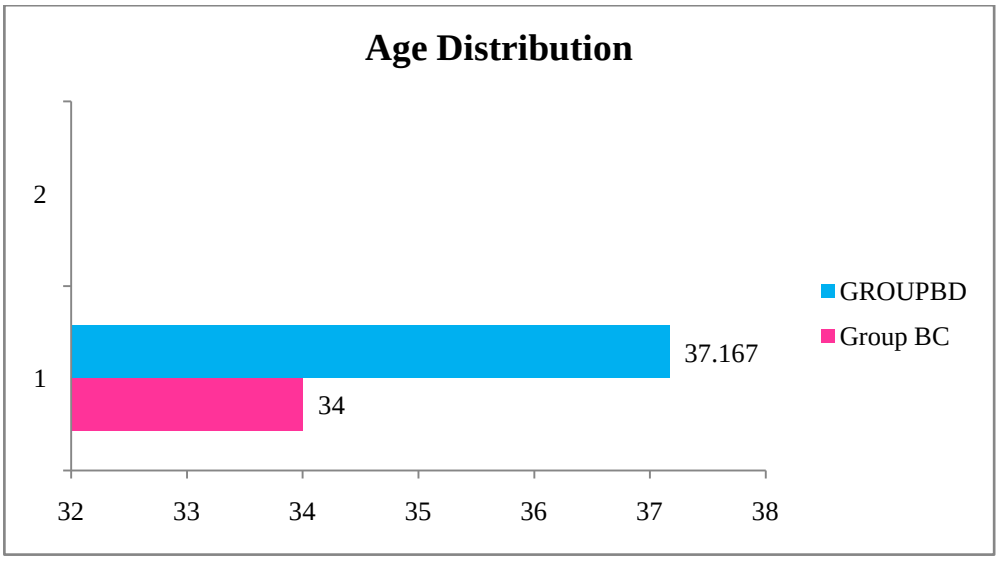
Sixty patients with ASAI and II of either sex between 15-50 years, posted for upper limb surgeries under brachial plexus block by supraclavicular approach were selected for the study. The study was to compare the efficacy of dexmedetomidine and clonidine with 0.357%bupivacaine for brachial plexus block by supraclavicular approach.

In both the groups adverse effects such as nausea, vomiting, hypoxemia and hypotension were not observed. Age, weight of the patent and duration of surgery between both the groups were comparable and were statistically not significant.($p>0.05$).

Table 1: age distribution between the two groups

	Mean	SD	p value	t value
Group BC	34.00	7.469	0.149	1.461
Group BD	37.167	9.229		

Fig 7 . Comparison of age (yrs) distribution between two groups

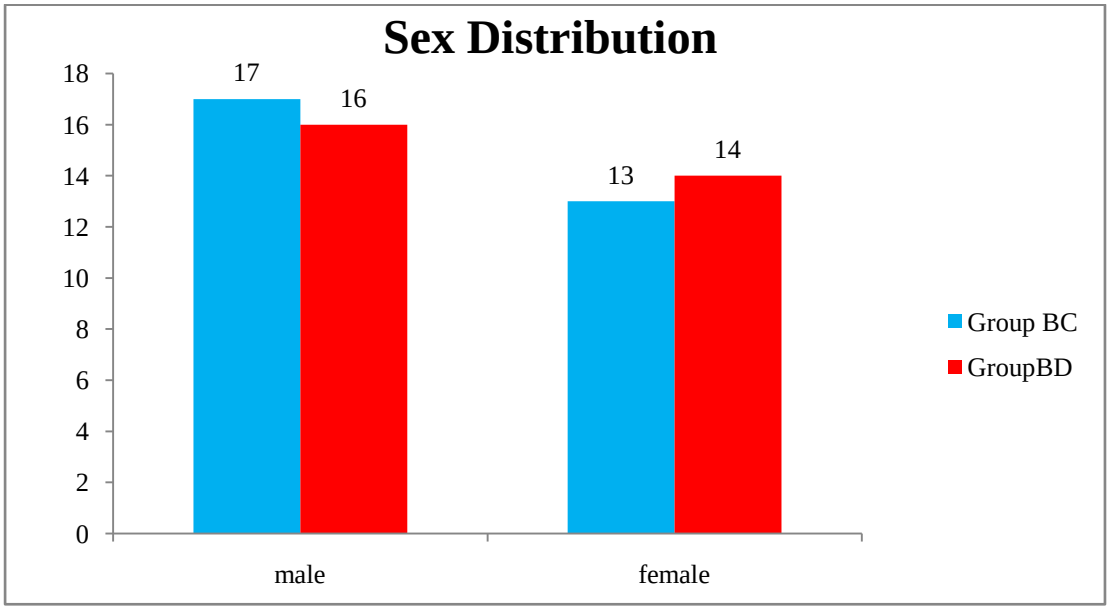


The mean age (yrs) of the group BC was 34_+7.4 years and the group BD was 37.1-+9.2 years. The age distribution of these two groups were statistically not significant (p>0.05)

Table 2: Comparision of sex distribution between the two groups

	Male	Female	Total
Group BC	17	13	30
Group BD	16	14	30
Total	33	27	60

Fig 8. Comparision of sex distribution between the two groups

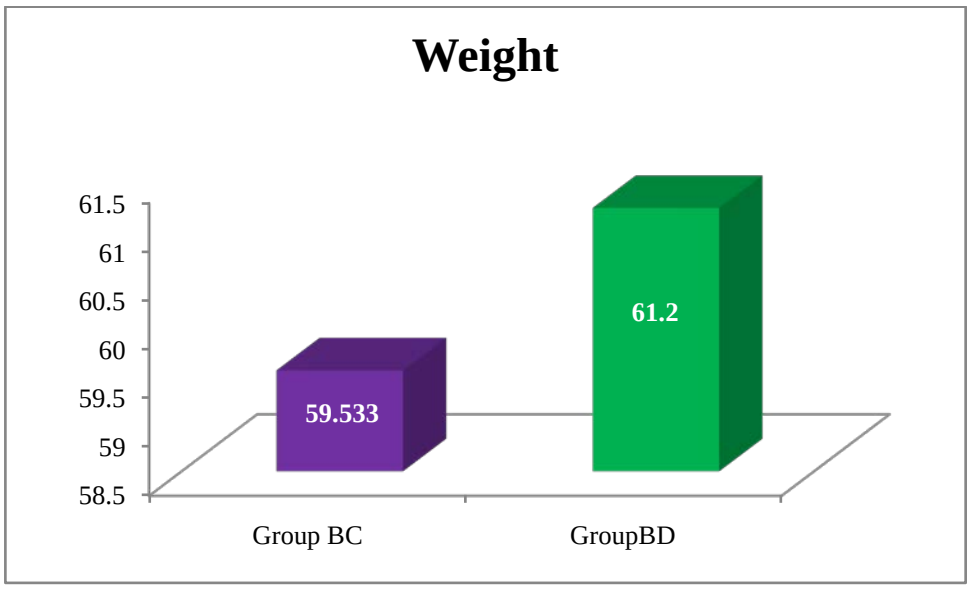


Comparison of sex distribution between the two groups were statistically not significant.

Table 3 comparison between weight (Kg) of the two groups

	Mean	SD	p value	t value
Group BC	59.533	5.981	0.301	1.043
GroupBD	61.2	6.386		

Fig 9 **comparison between weight (Kg) of the two groups**

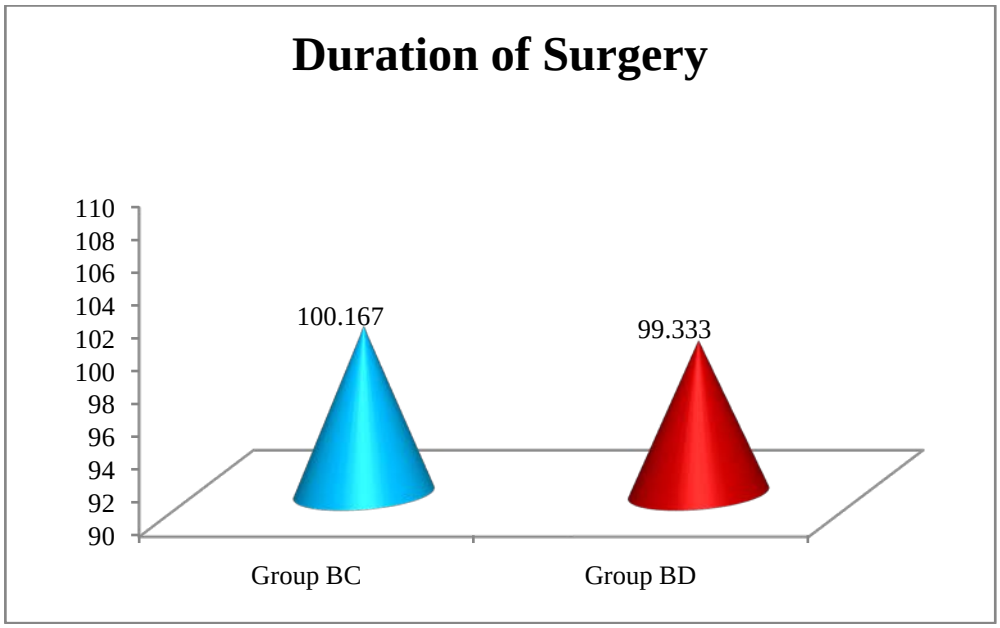


The mean weight of the group BC was 59.533kg, whereas the mean weight of the group BD was 61.2 kg. The difference in weight between the two groups were statistically not significant .($p>0.05$)

Table 4 Comparison of duration of surgery (min) among the two groups

	Mean	SD	p value	t value
Group BC	100.167	10.462	0.752	0.317
Group BD	99.333	9.890		

Fig 10 Comparison of duration of surgery (min) among the two groups

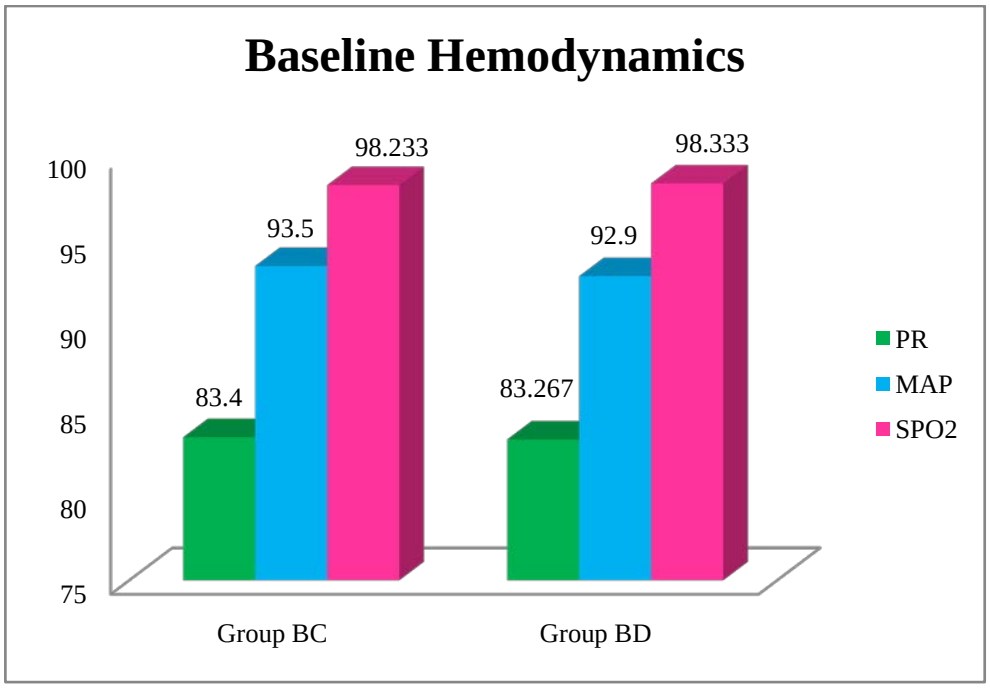


The mean duration of surgical procedure in group BC was 100.16 minutes and the mean duration of surgical procedure in group BD was 99.33minutes. The difference between the two groups were statistically not significant (p>0.05)

Table 5 comparison of baseline hemodynamic variables between the two groups

	Group BC		Group BD			
	Mean	**SD**	**Mean**	**SD**	**p value**	**t value**
PR	83.4	5.43	83.267	5.388	0.924	0.0985
MAP	93.5	6.474	92.900	6.375	0.719	0.362
SPO2	98.233	0.728	98.333	0.661	0.580	0.557

Fig 11. Comparison of baseline hemodynamic variables between the two groups

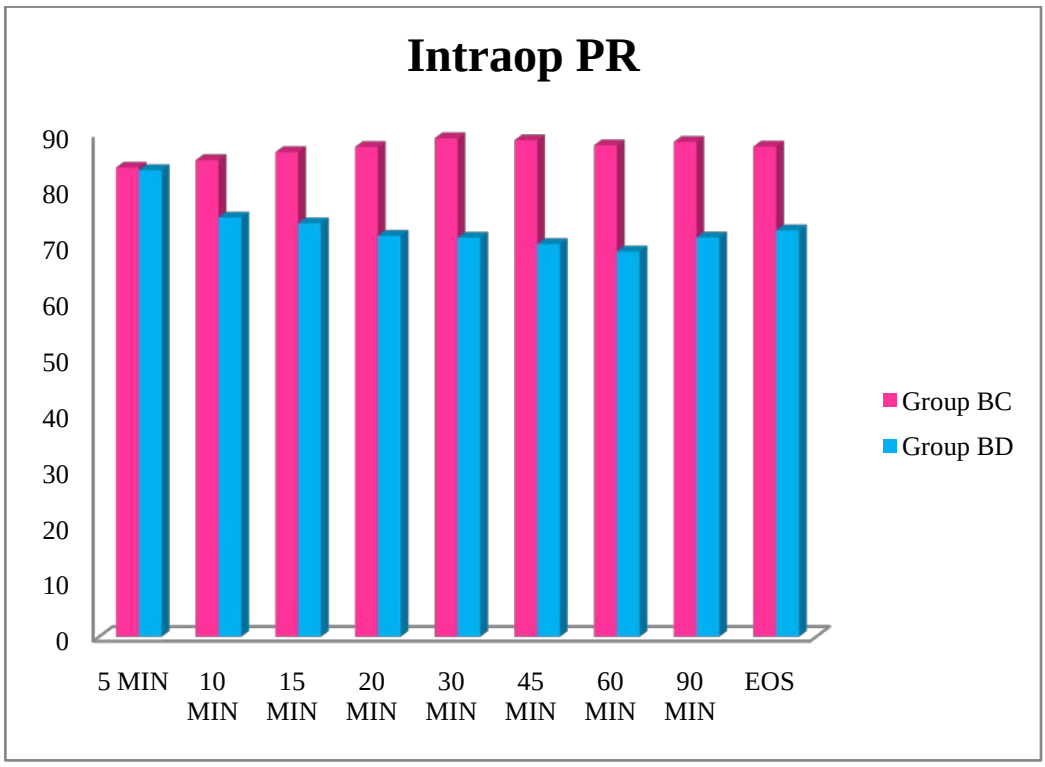


The pre operative hemodynamic variables among the two groups were statistically not significant.($p>0.05$)

Table 6Comparison of intraoperative pulse rate between two groups at various time intervals

	Group BC		Group BD		p value	t Value
	Mean	SD	Mean	SD		
5 MIN	83.900	5.189	83.433	5.380	0.734	0.342
10 MIN	85.233	5.380	74.933	4.226	0.001	8.246
15 MIN	86.667	6.013	73.900	4.221	0.001	9.518
20 MIN	87.600	5.922	71.667	5.707	0.001	10.610
30 MIN	89.167	5.427	71.333	3.898	0.001	14.618
45 MIN	88.800	5.774	70.167	2.902	0.001	15.794
60 MIN	87.900	6.525	68.867	2.636	0.001	14.814
90 MIN	88.500	5.551	71.367	2.619	0.001	15.290
EOS	87.667	5.492	72.633	5.707	0.001	13.483

Fig 12.Comparison of intraoperative PR between two groups at various time intervals

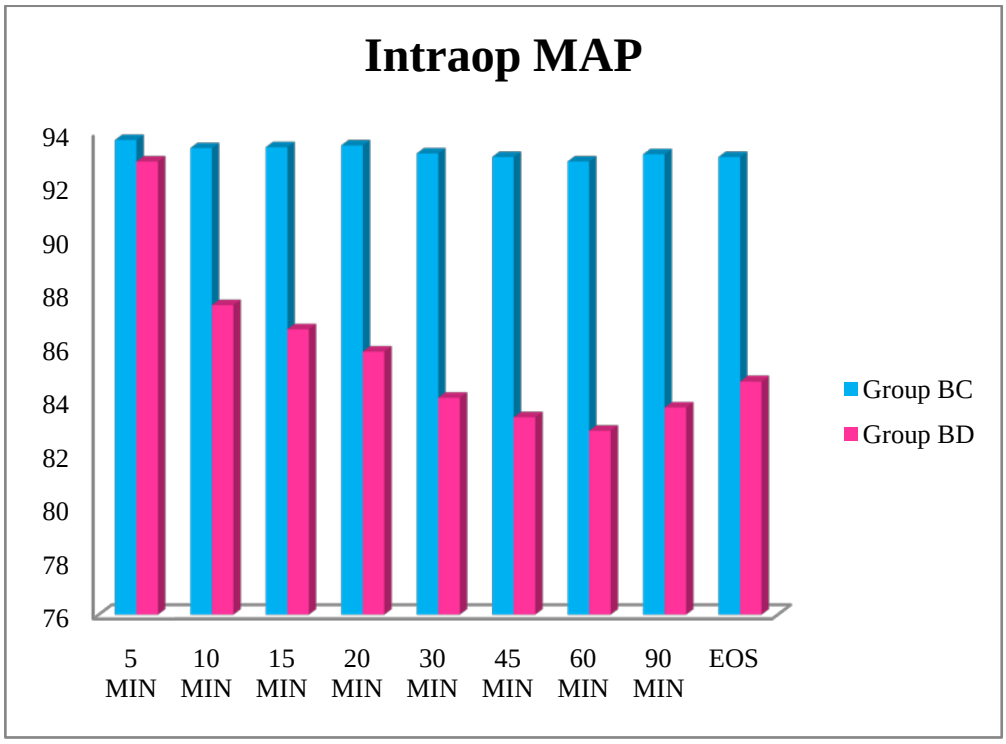


Except at 5th minute, the intraoperative pulse rate values were lower in Group **B**D, when compared to Group BC. This was statistically significant.($p<0.05$).

Table 7 Comparison of intra operative MAP between two groups at various time intervals

	Group BC		Group BD		p value	t Value
	Mean	**SD**	**Mean**	**SD**		
5 MIN	93.700	6.439	92.900	6.375	0.631	0.484
10 MIN	93.400	6.317	87.533	6.163	0.001	3.641
15 MIN	93.433	6.479	86.633	6.184	0.001	4.158
20 MIN	93.500	6.307	85.800	6.348	0.001	4.713
30 MIN	93.200	6.239	84.100	6.272	0.001	5.634
45 MIN	93.067	6.777	83.367	6.483	0.001	5.665
60 MIN	92.900	6.546	82.867	6.501	0.001	5.957
90 MIN	93.167	6.691	83.733	6.475	0.001	5.549
EOS	93.067	6.464	84.700	6.109	0.001	5.152

Fig 13. Comparison of intra operative MAP between two groups at various time intervals

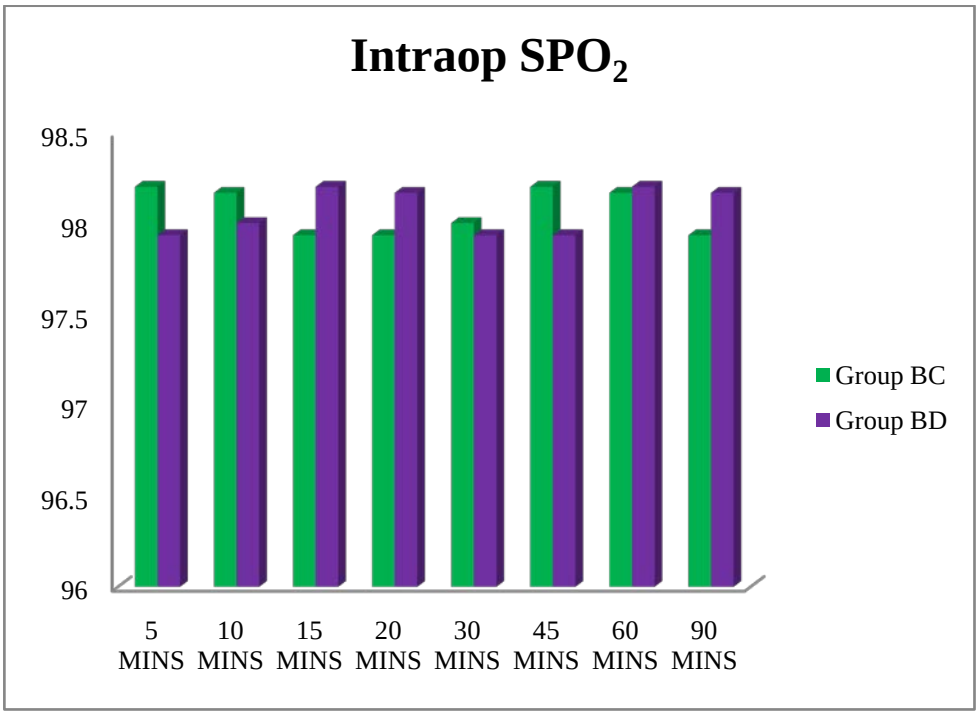


Except at the 5th minute, the intraoperative MAP values were lower in Group BD, when compared to Group **BC**. This was statistically significant ($p<0.05$).

Table 8 Comparison of intraoperative SPO2 between two groups at various time intervals

	Group BC		Group BD		p value	t Value
	Mean	**SD**	**Mean**	**SD**		
5 MINS	98.200	0.714	97.933	0.828	**0.187**	1.336
10 MINS	98.167	0.747	98.00	0.743	**0.390**	0.867
15 MINS	97.933	0.691	98.200	0.714	**0.147**	-1.469
20 MINS	97.933	0.828	98.167	0.747	**0.256**	-1.147
30 MINS	98.000	0.743	97.933	0.691	**0.720**	0.366
45 MINS	98.200	0.714	97.933	0.828	**0.187**	1.336
60 MINS	98.167	0.747	98.200	0.714	**0.860**	-0.177
90 MINS	97.933	0.691	98.167	0.747	**0.214**	-1.256
EOS	97.933	0.828	97.933	0.828	**1.000**	0

Fig 14.Comparison of intraoperative SPO_2 between two groups at various time intervals

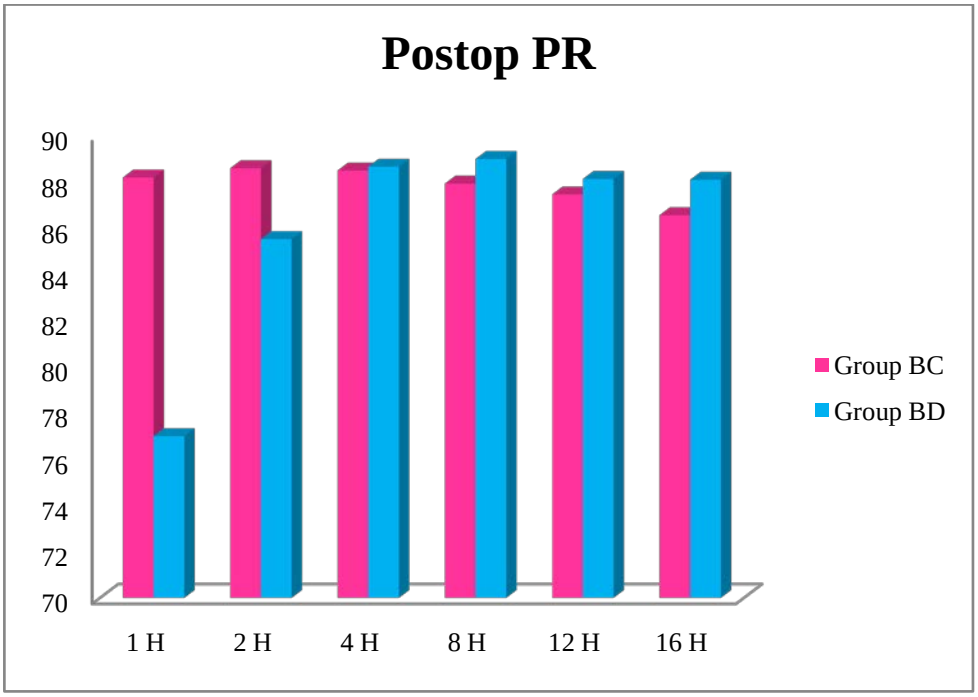


The mean intraoperative SPO2 among the two groups were statistically not significant.($p>0.05$)

Table 9 Comparison of postoperative pulse rate between the two groups

	Group BC		Group BD		p value	t Value
	Mean	**SD**	**Mean**	**SD**		
1 H	88.167	5.547	77.00	2.779	**0.001**	9.859
2 H	88.567	5.354	85.50	4.592	**0.021**	2.381
4 H	88.467	5.469	88.633	5.223	**0.904**	-0.121
8 H	87.900	5.435	88.967	5.461	**0.451**	-0.758
12 H	87.433	6.146	88.100	5.561	**0.661**	-0.441
16 H	86.533	6.410	88.067	5.942	**0.341**	-0.961

Figure 15. Comparison of postoperative pulse rate between the two groups



Post operative PR values in Group BD was lower than Group BC in the first postoperative hour($p<0.05$). In the 2H, 4H, 8H, 12H,16H values were statistically not significant.

Table 10 Comparison of Postoperative Mean arterial pressure between two groups

	Group BC		Group BD		p value	t Value
	Mean	SD	Mean	SD		
1 H	93.033	6.300	85.900	5.979	**0.001**	4.498
2 H	93.200	6.272	90.600	6.095	**0.109**	1.623
4 H	93.100	6.418	90.500	5.979	**0.156**	1.436
8 H	92.533	6.198	91.267	6.231	**0.433**	0.790
12 H	92.767	6.044	91.267	6.231	**0.347**	0.946
16 H	92.833	6.035	91.500	6.191	**0.402**	0.845

Fig 16. Comparison of Postoperative SPO2 between two groups

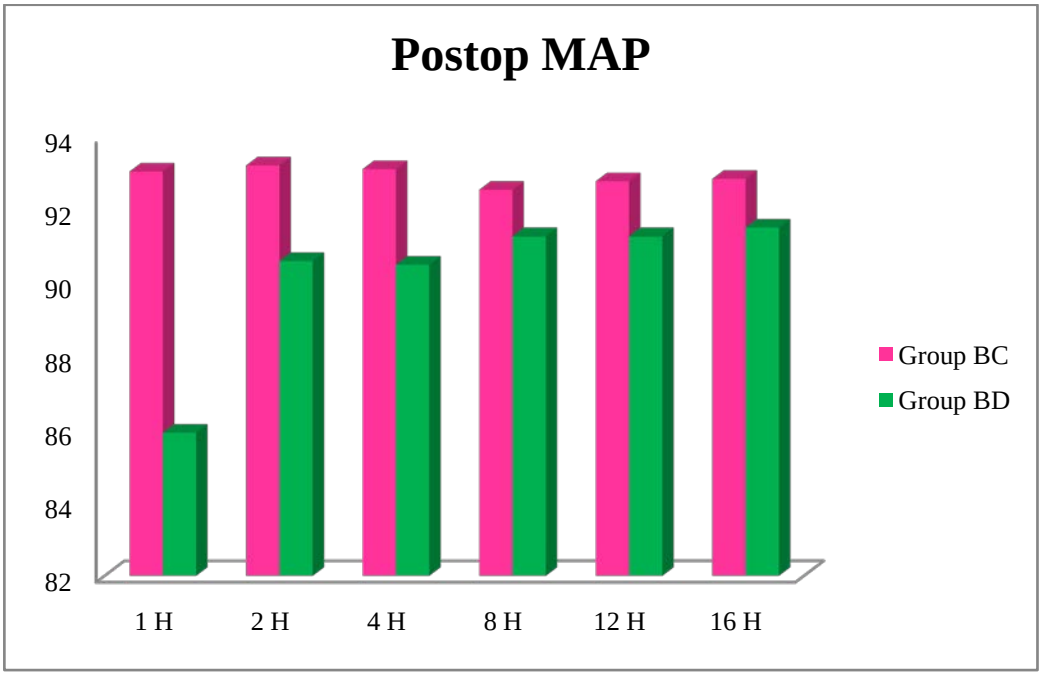
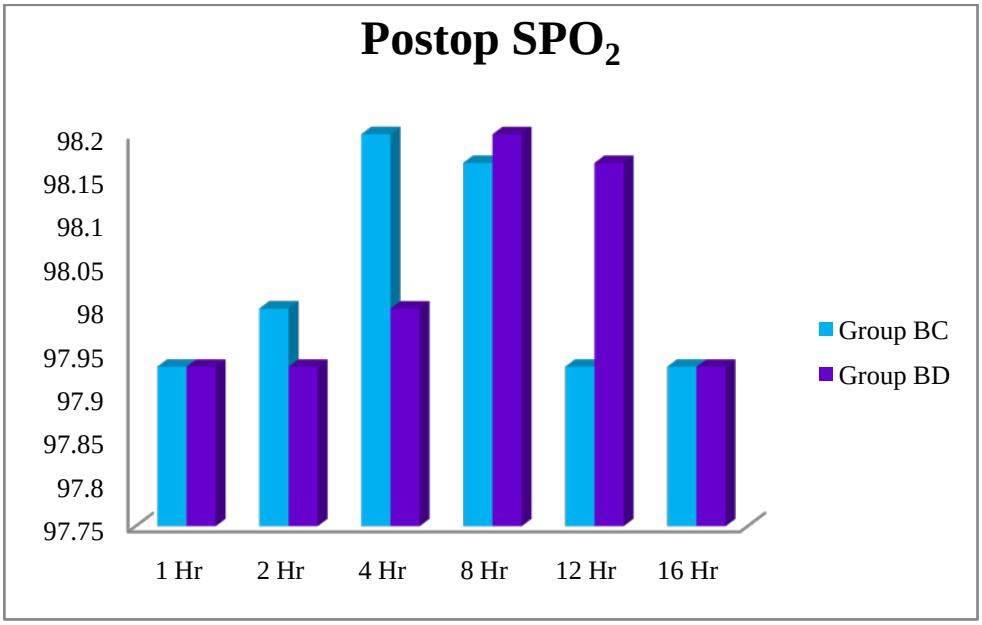


Table 11 Comparison of Postoperative SPO2 between two groups

	Group BC		Group BD		p value	t value
	Mean	SD	Mean	SD		
1 Hr	97.933	0.828	97.933	0.691	1.000	0
2 Hr	98.000	0.743	97.933	0.828	0.744	0.328
4 Hr	98.200	0.714	98.000	0.743	0.292	1.063
8 Hr	98.167	0.747	98.200	0.714	0.860	-0.177
12 Hr	97.933	0.828	98.167	0.747	0.256	1.147
16 Hr	97.933	0.828	97.933	0.691	1.000	0

FIG 17Comparison of Postoperative SPO2 between two groups

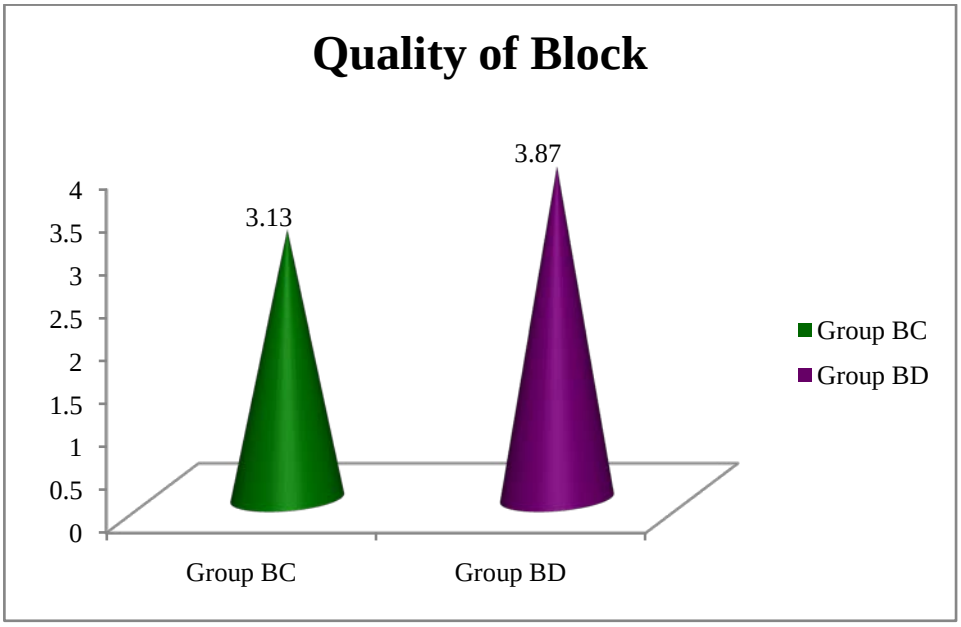


Post operative spo2 values between the two groups were statistically not significant.

Table 12 : Comparison of Quality Of Block Between Two Groups

Quality	Mean	SD	p value	t value	
Group BC	3.13	0.82	< 0.001	4.52	Significant
Group BD	3.87	0.35			

Figure 18- Comparison of Quality of Block Between Two Groups.

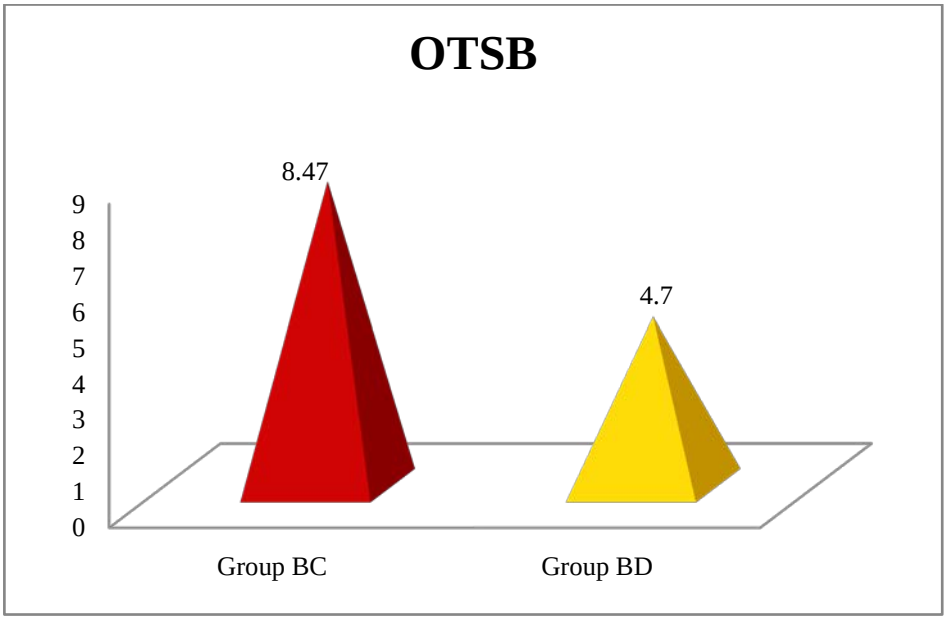


Bupivacaine dexmedetomidine group has better quality than bupivacaine clonidine group.

Table 13Comparison of onset time of sensory block(minutes)

	Mean	SD	p value	t value	
Group BC	8.47	1.04	< 0.001	17.19	Significant
Group BD	4.7	0.59			

Fig 19Comparison of onset time of sensory block(mt)

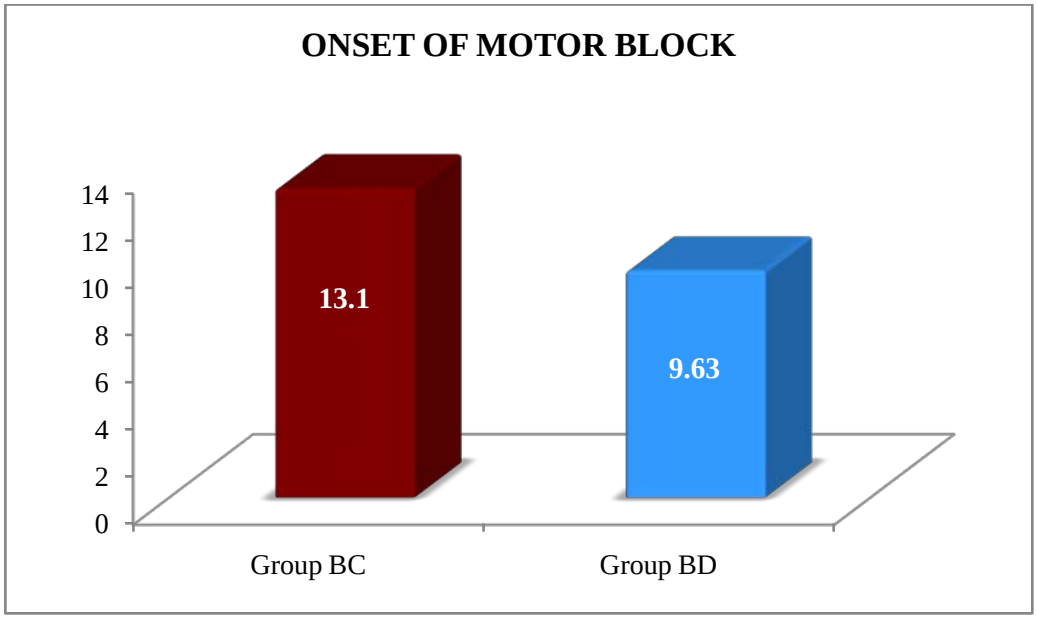


The mean time for onset of sensory block in Group BD was 4.7 minutes which was lower than Group BC -8.47 minutes. This was statistically significant($p<0.05$)

Table 14Comparison of onset time of motor block between two groups

OTMB	Mean	SD	p' value	t value	
Group BC	13.1	1.42	< 0.001	11.32	Significant
Group BD	9.63	0.89			

Fig 20 Comparison of onset time of motor block

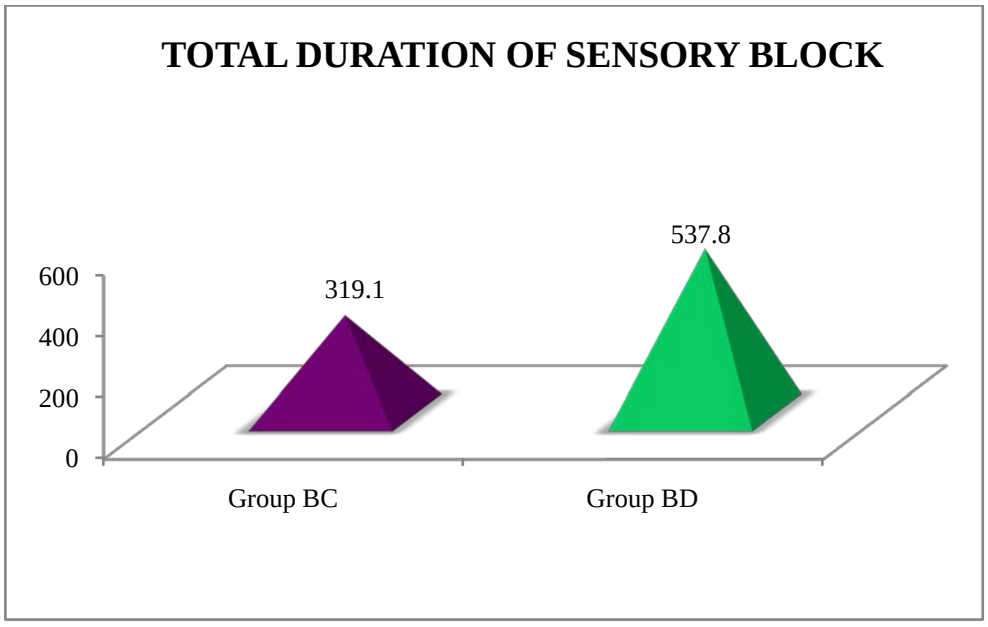


The mean time for onset of motor block in Group BD was 9.63 minutes which was lower than Group BC -13.1minutes.This was statistically significant($p<0.05$)

Table 15 Comparison of total duration of sensory block between two groups(mt)

TDSB	Mean	SD	p value	tvalue	
Group BC	319.1	32.74	< 0.001	25.89	Significant
Group BD	537.8	32.67			

Fig 21Comparison of total duration of sensory block between two groups(mt)

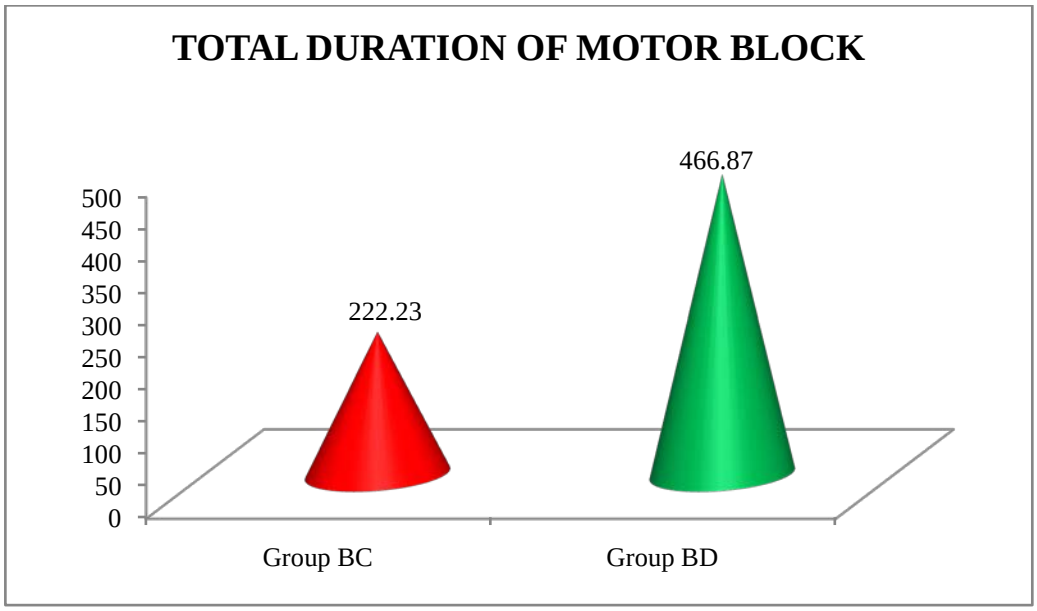


The mean time for total duration of sensory block in Group BD was 537.8minutes. This was higher than the Group BC -319.1minutes.It was statistically significant ($p<0.05$).

Table 16 Comparison of total duration of motor block between two groups

TDMB	Mean	SD	p value	t value	
Group BC	222.23	17.84	< 0.001	40.27	
Group BD	466.87	28.08			Significant

Fig 22Comparison of total duration of motor block between two groups(mts)

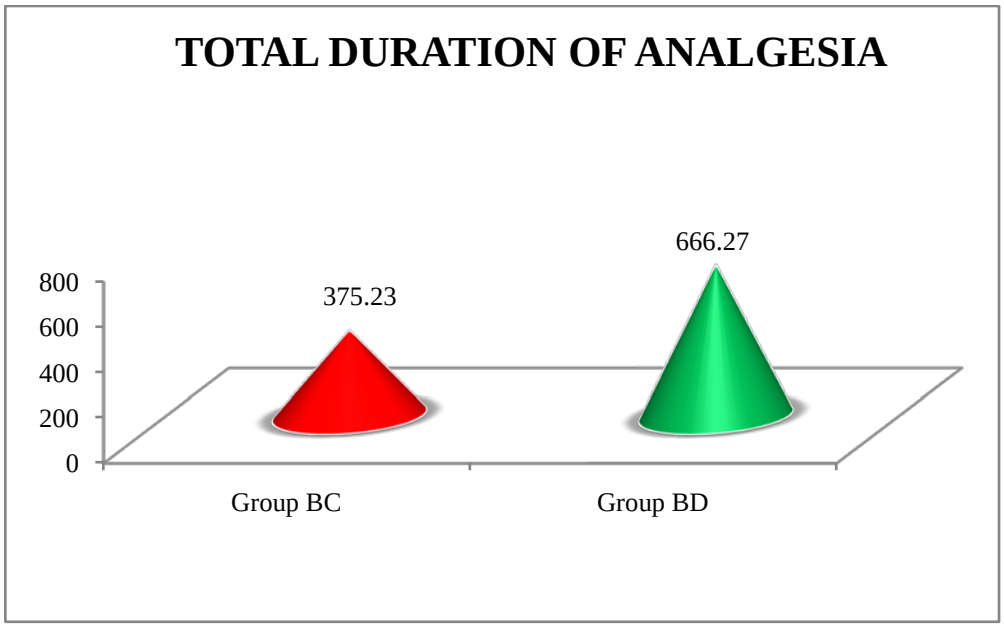


The mean time for total duration of motor block in Group BD was 466.87minutes. This was higher than in Group BC 222.23 minutes. It was statistically significant ($p<0.05$)

Table 16Comparison of total duration of analgesia between two groups

DOA	Mean	SD	p value	t value	
Group BC	375.23	32.6	< 0.001	32.55	Significant
Group BD	666.27	36.54			

Fig 23Comparison of total duration of analgesia between two groups



The total duration of Analgesia in Group **B**D was 666.27 minutes. This was higher than in Group BC – 375.23 minutes. It was statistically significant. ($p<0.05$).

DISCUSSION

Brachial plexus block provides post operative analgesia of short duration, even when a long acting local anaesthetic like bupivacaine is used alone. Various adjuvants like opioids, midazolam, neostigmine, vasoconstrictors, sodium bicarbonate, dexamethasone have been used as an adjuvant with local anesthetics to prolong the time of analgesia,but they may have unwanted side effects or may be ineffective . The alpha 2 agonists dexmedetomidine and clonidine are known to have analgesic effect and also enhance the effect of local anaesthetics intrathecally and epidurally. Alpha2 agonists produce this effect by its action on alpha 2 adrenergic receptors found in peripheral nerves.

Here an attempt has been made to compare the efficacy of dexmeditomidine and clonidine as an adjuvant to bupivacaine 0.375%in brachial plexus block (supraclavicular approach) in terms of onset time,duration of analgesia and sedation. Hemodynamic variables and supplementary analgesic requirements in first 24 hours were also studied.

The duration of analgesia was calculated from the end of local anaesthetic injection to the first complaint of pain. Following adverse effects were noted in the intraoperative and postoperative period.

* Hypotension (less than 20% reduction in MAP)
* Bradycardia (less than 50 bpm)
* Hypoxemia (Spo2 less than 90%)
* Nausea and vomiting.

The α 2 agonists dose dependently enhance local anaesthetic potency and prolong its duration by combining at the α 2 receptors at the peripheral level. The other possible mechanisms by which the α 2 agonists improve local anaesthetic action include

1. Vasoconstriction around the site of injection. Thus the absorption of local anaesthetic drug will be delayed, resulting in the prolongation of the local anaesthetic effect.
2. A direct action on the peripheral nerve. Clonidine directly inhibits peripheral nerve action.

Clonidine and Dexmedetomidine are the currently used α 2 receptor agonists. The usage of clonidine in brachial plexus block with various local anaesthetics yield conflicting results. It was found that clonidine prolongs the motor blockade with mepivacaine and bupivacaine but not with ropivacaine.

The reason for this effect may be because that ropivacaine itself has an intrinsic vasoconstrictor effect and addition of clonidine to ropivacaine did not increase this vasoconstriction effect. Dexmedetomidine has been found to be an effective and safe adjuvant in many studies on neuraxial and peripheral nerve blocks.

SUMMARY

In adult patients undergoing orthopaedic forearm and hand surgeries under brachial plexus block, the addition of 2μg/kg of dexmedetomidine to 35 ml of bupivacaine (0.357%) produces a shorter onset time for sensory and motor blockade. It also prolongs the duration of sensory and motor blockade. Postoperatively the duration of analgesia is prolonged with minimal reduction in pulse rate, blood pressure.

CONCLUSION

The addidition of Dexmedetomidine (2μg/kg) to bupivacaine (0.357%) in brachial plexus block by supraclavicular approach results in a shorter onset time for sensory and motor blockade, prolongs the duration of sensory and motor blockade and also the duration of analgesia.

ஆராய்ச்சி ஒப்புதல் கடிதம்

நோயாளியின் பெயர்: வயது: பாலினம்: வார்டு:

முகவரி: வியாதி:

மருத்துவஎண்: அறுவைசிகிச்சை:

எனக்கு கையில் அறுவை சிகிச்சை செய்து கொள்வதற்காக கைக்குச் செல்லும் நரம்பு மண்டலத்தில் மயக்க மருந்து செலுத்திக் கொள்ள சம்மதிக்கிறேன். அந்த மயக்க மருந்தோடு டெக்ஸ்மெடிட்டோமிடின் அல்லது குளோனிடின் என்னும் ஆராய்ச்சி மருந்தை சேர்த்து செலுத்திக் கொள்ள சம்மதிக்கிறேன். இதனால் ஏற்படும் நன்மை தீமைகளை மயக்க மருத்துவர் மூலம் அறிந்து கொண்டு என் முழு சம்மதத்துடன் யாருடைய நிர்ப்பந்தமுமின்றி இந்த ஆராய்ச்சிக்கு ஒப்புதல் அளிக்கிறேன்.

இப்படிக்கு

நோயாளியின் கையொப்பம்:

தேதி:

கழுத்துப்பகுதியில் கைக்கு செல்லும் நரம்பு மண்டலத்தில் பியுபிவிக்கேன் மற்றும் டெக்ஸ்மெடிடோமிடின் அல்லது குளோனிடின் மருந்தை செலுத்துவதற்கான ஒப்புதல் படிவம்

பெயர்: வயது: இனம்: ஆண்/பெண்

மருத்துவஎண்: வார்டு: வியாதி:

அறுவைசிகிச்சை:

விளக்கம்:

கையில் அறுவைசிகிச்சை செய்யும் போது, கழுத்துப்பகுதியில் உள்ள கைக்கு செல்லும் நரம்பு மண்டலத்தில், புபிவாகையின் என்னும் மயக்க மருந்தினை ஊசியின் மூலம் செலுத்துவது கையை உணர்விழக்க செய்யும் முறைகளில் ஒன்றாகும். இதனால் அறுவை சிகிச்சை செய்யும் போது கை உணர்ச்சியற்று இருக்கும். புபிவாகையின் என்னும் மயக்க மருந்தோடு டெக்ஸ்மெடிடோமிடின் அல்லது குளோனிடின் (ஆல்பா 2 அகோனிஸ்ட்) என்னும் ஆராய்ச்சிக்கான மருந்தை செலுத்துவதினால் ஏற்படும் பயன்கள், பின்விளைவுகள் தெளிவாக விளக்கி கூறப்பட்டது.

பயன்கள்:

புபிவாகையின் மருந்தோடு டெக்ஸ்மெடிடோமிடின் அல்லது குளோனிடின் மருந்தை சேர்த்து கொடுக்கும் போது,

- சீக்கிரமாக கை உணர்ச்சியற்றுபோகும்.
- அறுவைசிகிச்சை முடிந்த பின்னர் கூடுதல் நேரம் கையில் வலி இல்லாமல் இருக்கும்.

மாற்றுசிகிச்சை:

கழுத்துப்பகுதியில் மயக்க மருந்தினை செலுத்தாமல், முழு மயக்கம் (ஜெனரல் அனஸ்தீஸியா) கொடுத்து அறுவைசிகிச்சை செய்யும் முறை பற்றி எனக்கு தெரிவிக்கப்பட்டது.

பின்விளைவுகள்:

மயக்க மருந்தினை செலுத்தும் போது பின்வரும் பின்விளைவுகள் பற்றி எனக்கு தெரிவிக்கப்பட்டது.

- ❖ மயக்க மருந்தை கழுத்துப் பகுதியில் செலுத்தும் போது, அது தற்செயலாக இரத்த நாளங்களுக்குள் சென்று தலைசுற்றுதல், படபடப்பு, இதயத்தின் துடிப்பு அதிகமாகுதல், மயக்கம் அடைதல், வலிப்பு போன்றவை வரலாம். அந்த பாதிப்புகள் மருந்துகள் மூலம் சரிசெய்யப்படும்.
- ❖ டெக்ஸ்மெடிடோமிடின் மற்றும் குளோனிடின் இதய துடிப்பின் அளவையும், இரத்த அழுத்தத்தையும் குறைக்கலாம். வாந்திஏற்படுத்தலாம். அதற்கு தக்க மாற்று மருந்துகள் தரப்படும்.

அறுவைசிகிச்சைக்கான ஒப்புதல்:

- o எனக்கு நன்கு புரிகின்ற மொழியில் தமிழில் எனது வலது/இடது கையில் அறுவைசிகிச்சை செய்யும் போது மயக்க மருந்தான புபிவாகையின் மற்றும் டெக்ஸ்மெடிடோமிடின் அல்லது குளோனிடின் மருந்தினை கழுத்துப்பகுதியில் செல்லும் நரம்பு மண்டலத்தில் செலுத்துவதற்கான முறை மற்றும் காரணம், பயன்கள், பின்விளைவுகள், பற்றி எனக்கு விளக்கப்பட்டது. நான் அதை புரிந்து கொண்டேன். யாருடைய நிர்ப்பந்தமுமின்றி இந்த மயக்க மருந்து செலுத்தும் முறைக்கு நான் ஒப்புதல் அளிக்கிறேன்.
- o எனக்கு இந்தமயக்கமருந்தைசெலுத்தும் போது எதிர்பாராத நிலைமை **வெளிப்படலாம்** என்பது பற்றியும் அதற்கு தேவைப்படும் கூடுதல் / எதிர்பாராத அவசர சிகிச்சை முறைகள் செய்ய வேண்டியது வரலாம் என்பது பற்றியும் விளக்கப்பட்டது. எனவே மருத்துவர் தேவையெனக் கருதும் மாற்று மருந்துகள் செலுத்தவும் மற்றும் சிகிச்சை முறைகள் செய்யவும் நான் அனுமதி அளித்து விண்ணப்பிக்கிறேன்.
- o எனக்கு அளிக்கப்படும் இந்த சிகிச்சை முறையை எனது அடையாளம் அல்லது விபரங்கள் தெரியாத வகையில் பிறர் பார்வையிடவும், புகைப்படம், வீடியோ எடுக்கவும் அனுமதிப்பதுடன் அவற்றை மருத்துவத்திற்கும்,

ஆராய்ச்சிக்கும் மற்றும் பயிற்சிக்கும் பயன்படுத்திக் கொள்ள ஒப்புதல் அளிக்கிறேன்.

- எனக்கு கேள்விகள் கேட்பதற்கு வாய்ப்பு அளிக்கப்பட்டது. அதற்கான விளக்கமும் தரப்பட்டது. இந்த ஒப்புதல் படிவத்தை நான் படித்து பார்த்து அதன் விபரங்களை அறிந்து யாருடைய தூண்டுதலின்றி எனது சுய விருப்பத்துடன் இந்த படிவத்தில் கையொப்பம் செய்துள்ளேன்.

நோயாளி /உறவினர் கையொப்பம்:

பெயர்:

உறவுமுறை: தேதி:

மருத்துவர் தீர்மானஅறிவித்தல்:

நான் இந்த மயக்கமருந்துகள் செலுத்தப்படும் விதம், விளைவுகள், பாதிப்புகள், பயன்கள் மற்றும் மாற்று முறைகள் பற்றி விளக்கியுள்ளேன் என்பதை இதன் மூலம் தெரிவிக்கின்றேன். நான் நோயாளிக்கு கேள்வி கேட்பதற்கான வாய்ப்பை கொடுத்து அதற்கு பதில் அளிக்கிறேன்.

மருத்துவரின் கையொப்பம்:

மருத்துவரின் பெயர்: தேதி:

சாட்சி விபரம்:

கையொப்பம்:

பெயர்: தேதி:

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PROFORMA

Case NO- **I.P-no-**

NAME :

ADDRESS :

AGE :

SEX :

D.O.ADMISSION :

HISTORY IN BRIEF :

CLINICAL DIAGNOSIS/ INDICATION :

<u>EXAMINATION IN BRIEF :</u>

- **Vitals**
  - **PULSE**
  - **B.P-**
  - **AIRWAY-ASSESSMENT**
- **SYSTEMIC EXAMINATION**
- **BASELINE HAEMODYNAMICS :**
  - **PR:**
  - **BP:**
  - **SPO2:**

INVESTIGATIONS

* **COMPLETE BLOOD COUNT**
* **RBS**
* **BLOOD UREA SERUM CREATININE**
* **BT CT**

URINE EXAMINATION- ALBUMIN SUGAR MICROSCOPY

CHEST X-RAY :

ECG :

ASA GRADING :

SURGICAL PROCEDURE :

DURATION :

PARAMETERS OBSERVED-

1. **Onset time for sensory block -**
2. **Onset time for motor block -**
3. **Total duration of sensory block -**
4. **Total duration of motor block -**
5. **Duration of analgesia -**

Adverse Effects

* Nausea +/-
* Vomiting +/-
* Bradycardia+/-
* Hypotension +/-
* Hypoxemia +/-

Intra operative monitoring

Time After Block	PR	MAP	SPO2
5min			
10min			
15 min			
20 min			
30 min			
45 min			
60 min			
90 min			
EOS			

Post operative monitoring

Time After Surgery	PR	MAP	SPO2
1H			
2H			
4H			
8H			
12H			
16H			

GROUP BUPIVACAINE - CLONIDINE

S.NO	AGE	SEX	WT	TYPE OF SURGERY	BASELINE PR 5MT	MAP	SPO2	INTRAOP PR 5MT	10	15	20	30	45	60	90	EOS	INTRA OP MAP 5MT	10	15	20	30	45	60	90	EOS	INTRA OP SPO2 5MT	10 MT	15	20	30	45	60	90	EOS	DOS	POSTOP PR 1H	2H	4H	8H	12H	16H	POSTOP MAP 1H	2H	4H	8H	12H	16H	POSTP SPO21H	2H	4H	8H	12H	16H	Quality	OTSB mt	OTMB	TDSB	TDMB	DOA
1	40	F	61	k wire fixation	88	98	99	88	90	94	90	92	94	95	96	97	98	97	96	98	98	97	96	96	96	97	98	98	97	98	97	98	98	97	120	97	96	95	93	92	90	95	96	97	95	96	96	97	98	97	98	98	97	3	7	14	260	210	356
2	29	F	64	orif with plate osteosynthesis	86	97	97	87	88	90	91	93	96	89	88	90	97	97	98	99	98	97	97	97	97	98	99	98	98	97	98	99	98	98	115	90	88	89	91	93	95	96	95	96	95	96	96	98	97	98	99	98	98	2	8	13	276	204	341
3	33	F	53	orif with asian dcp	80	98	98	83	85	88	90	92	94	95	93	90	98	98	99	97	97	98	98	98	98	98	97	97	99	98	98	97	97	99	100	90	90	92	93	91	93	97	98	97	96	97	97	99	98	98	97	97	99	3	8	14	305	242	360
4	37	M	50	orif with plate osteosynthesis	86	98	98	86	88	89	90	92	92	93	94	95	98	98	99	100	97	98	98	99	99	98	99	99	97	98	98	99	99	97	90	95	96	97	94	93	92	98	99	100	99	99	99	97	98	98	99	99	97	4	7	12	355	203	403
5	25	M	52	deroofing and curettage	87	83	99	88	89	90	91	92	91	94	92	90	83	85	84	84	83	82	83	83	85	98	98	98	97	97	98	98	98	97	95	90	92	93	94	95	96	82	83	81	82	82	82	97	97	98	98	98	97	2	9	14	286	200	307
6	34	M	59	orf with plating	79	98	98	79	80	82	81	84	86	83	87	80	98	97	96	97	99	99	98	98	98	99	99	99	98	97	99	99	99	98	135	80	84	82	78	78	77	98	99	100	99	100	99	98	97	99	99	99	98	4	9	14	358	236	410
7	39	F	57	buttress plating with k wire fixation	76	99	99	76	79	80	78	84	86	87	88	84	99	99	100	99	97	98	99	99	99	98	98	98	99	98	98	98	98	99	90	84	85	87	88	89	90	98	97	96	95	94	96	99	98	98	98	98	99	4	7	12	320	205	384
8	34	M	67	orif with asian dcp	89	98	98	89	90	93	94	95	93	92	90	90	98	98	99	100	98	99	98	99	98	97	99	98	99	98	97	99	98	99	95	90	91	92	93	95	96	99	100	99	98	97	98	99	98	97	99	98	99	4	10	15	342	228	418
9	34	F	69	orif with plate osteosynthesis	80	100	97	81	80	84	83	84	83	88	89	90	100	99	100	99	98	99	98	99	98	98	97	97	97	99	98	97	97	97	110	90	90	88	85	86	83	98	97	99	98	98	98	97	99	98	97	97	97	4	11	15	356	231	388
10	48	M	63	orif with narrow dcp	88	102	98	88	90	94	93	95	92	90	89	90	102	102	103	102	100	101	101	102	100	99	97	98	99	99	99	97	98	99	105	90	88	90	91	87	86	100	100	99	98	98	98	99	99	99	97	98	99	3	9	13	312	220	376
11	22	F	60	ORIF with k wire fixation	83	95	99	83	85	84	87	90	92	90	90	88	95	96	97	96	94	95	95	96	95	98	97	98	99	97	98	97	98	99	100	88	90	91	92	93	86	95	94	93	94	95	95	99	97	98	97	98	99	3	9	14	302	236	386
12	26	M	51	ORIF with asian DCP	78	92	98	78	80	79	80	82	80	78	79	80	97	93	90	91	93	94	93	92	92	98	99	98	97	99	98	99	98	97	90	80	81	78	77	76	7	92	93	94	92	92	92	97	99	98	99	98	97	2	8	12	289	203	334
13	34	F	65	ORIF with plate osteosynthesis	72	94	98	73	74	78	80	84	88	84	83	82	94	95	94	93	95	92	93	93	94	99	99	99	98	99	99	99	99	98	90	82	82	80	78	77	79	94	94	93	93	93	93	98	99	99	99	99	98	2	9	14	276	208	322
14	38	M	68	orif with narrow dcp	84	93	99	84	85	88	90	89	86	87	88	88	93	92	92	93	95	94	93	92	92	99	98	98	98	97	99	98	98	98	90	88	90	89	88	90	90	92	91	90	90	91	91	98	97	99	98	98	98	4	10	15	348	256	402
15	24	M	66	orif with plate osteosynthesis	89	96	99	89	90	92	93	94	90	94	93	93	96	96	95	94	92	94	96	98	98	99	98	97	98	97	98	98	99	97	100	93	94	95	96	95	94	95	94	95	94	95	94	97	98	98	98	99	97	4	9	14	318	210	396
16	30	F	54	ORIF with plate osteosynthesis	83	97	98	84	88	89	90	92	96	98	94	93	97	96	97	96	98	97	97	98	97	99	99	97	99	97	99	99	97	99	95	96	97	95	93	92	90	96	97	96	96	96	96	99	97	99	99	97	99	3	8	12	305	207	386
17	32	F	56	k wire fixation	90	99	99	90	92	93	95	94	92	95	96	96	99	100	99	98	99	98	99	99	99	98	98	97	99	98	98	98	97	99	90	98	98	97	95	93	90	99	100	99	98	98	98	99	98	98	98	97	99	3	8	13	300	203	376
18	36	M	59	ORIF With plate osteosynthesis	92	90	98	92	91	90	88	89	93	94	96	98	90	89	88	90	89	90	89	89	90	97	98	97	98	98	97	98	97	98	110	98	98	96	90	87	85	90	89	88	90	90	98	98	98	97	98	97	98	4	7	11	366	268	396
19	42	F	53	orif with asian dcp	88	94	97	88	90	9	92	93	96	97	98	90	94	95	96	95	93	95	95	95	99	99	99	98	97	98	99	99	98	97	100	90	88	90	87	86	85	95	94	95	94	93	94	97	98	99	99	98	97	2	9	14	288	198	340
20	47	M	56	orif with plate osteosynthesis	72	82	99	74	76	77	75	76	78	79	80	78	83	82	84	85	81	80	80	80	80	99	98	99	98	98	99	98	99	98	90	78	77	80	84	83	80	80	81	82	80	80	80	98	98	99	98	99	98	4	8	12	334	238	398
21	32	F	52	orif with narrow dcp	76	90	98	78	76	74	78	80	77	75	79	80	90	92	93	91	93	89	90	9	90	98	97	97	99	98	98	97	97	99	95	89	84	78	80	74	72	93	90	91	92	89	90	99	9	9	97	97	99	3	9	14	328	225	386

S.NO	AGE	SEX	WT	TYPE OF SURGERY	BASELINE PR 5MT	MAP	SPO2	INTRAOP PR 5MT	10	15	20	30	45	60	90	EOS	INTRA OP MAP 5MT	10	15	20	30	45	60	90	EOS	INTRA OP SPO2 5MT	10 MT	15	20	30	45	60	90	EOS	DOS	POSTOP PR 1H	2H	4H	8H	12H	16H	POSTOP MAP 1H	2H	4H	8H	12H	16H	POSTP SPO21H	2H	4H	8H	12H	16H	Quality	OTSB mt	OTMB	TDSB	TDMB	DOA
22	38	M	58	oblique osteotomy and k wire fixation	86	84	99	89	88	86	87	89	85	83	89	89	84	83	84	83	82	83	83	83	82	98	98	97	98	99	98	98	97	98	100	90	92	87	88	90	86	83	84	84	84	85	84	98	99	98	9	97	98	2	9	14	357	240	394
23	34	M	60	orif with plate osteosynthesis	87	95	97	87	90	88	89	92	97	80	88	86	95	94	93	94	94	93	93	93	93	97	97	97	98	97	97	97	97	96	95	86	88	87	86	85	84	95	96	95	94	95	95	96	97	97	97	97	96	3	9	15	296	205	346
24	24	M	53	orif with dcp	80	96	99	80	78	76	80	84	80	82	84	83	96	95	94	95	94	92	95	94	95	99	98	98	98	99	99	98	98	98	105	83	85	88	85	80	82	95	97	96	95	94	95	98	99	99	98	98	98	2	8	12	287	215	308
25	33	M	69	orif	86	100	99	86	85	###	92	88	88	87	87	86	100	99	98	99	100	100	98	99	98	99	98	98	97	99	99	98	98	97	100	86	88	90	92	93	90	98	98	99	98	99	98	97	99	99	98	98	97	3	7	10	306	232	378
26	21	M	70	orif with asian dcp	79	82	98	99	83	85	90	87	83	76	77	78	82	8	80	81	83	80	81	82	82	98	99	98	98	98	98	99	98	98	110	78	80	82	83	85	87	82	83	82	81	82	82	98	98	98	99	98	98	4	7	11	352	229	426
27	33	M	65	orif with plate osteosynthesis	80	97	97	80	82	83	84	85	86	87	85	84	97	96	95	96	98	97	97	98	98	97	98	99	98	97	97	98	99	98	90	84	85	87	88	89	90	98	98	97	98	99	98	98	97	97	98	99	98	3	10	15	343	218	380
28	50	F	61	orif with narrow dcp	80	80	99	80	82	84	85	88	83	82	84	86	80	89	80	8	81	80	79	80	80	99	98	98	98	99	99	98	98	98	100	86	87	88	89	90	88	82	81	80	81	82	82	98	99	99	98	98	98	4	8	11	380	243	418
29	28	F	56	orif with plate osteosynthesis	89	97	98	89	90	96	97	95	92	88	85	86	97	96	98	98	94	96	96	95	96	98	97	98	98	98	98	99	98	98	105	86	85	84	80	78	76	96	97	98	96	96	96	98	98	98	99	98	98	4	8	12	354	228	402
30	43	M	59	orif with plate osteosynthesis	89	81	98	89	93	95	97	99	95	95	94	90	81	83	82	81	82	80	81	80	80	99	99	98	98	98	99	99	98	98	95	90	88	87	86	88	90	80	81	82	80	82	82	98	98	99	99	98	98	2	9	12	274	226	340

GROUP BUPIVACAINE - DEXMEDETOMIDINE

S.no	Age	Sex	Wt	Type of Surgery	Baseline PR	MAP	SPO2	Intra op PR 5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	Intraop map5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	intraopspo2 5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	duraton of surgery mt	postop pr 1h	2h	4h	8h	12h	16h	postopmap 1h	2h	4h	8h	12h	16h	postopspo21h	2h	4h	8h	12h	16h	quality	OTSB	OTMB	TDSB	TDMB	DOA
1	30	F	57	ORIF with plate osteosynthesis	76	98	99	77	71	68	59	83	78	73	71	74	98	92	91	90	89	89	88	88	89	98	97	99	99	99	98	99	99	98	100	79	86	95	93	92	90	90	95	95	94	95	96	99	98	97	99	99	99	3	4	9	478	418	640
2	50	F	65	k wire fixation	86	89	99	85	76	76	73	67	66	64	68	73	89	84	83	82	80	79	79	80	82	99	98	98	98	98	99	98	98	99	90	80	94	95	96	95	94	83	87	87	88	88	83	98	99	98	98	98	98	4	4	9	484	420	647
3	40	M	69	ORIF with plate osteosynthesis	87	93	98	87	78	78	77	73	72	70	72	71	93	88	87	86	84	83	82	82	83	99	98	97	99	98	99	97	99	99	95	78	88	90	87	86	85	84	90	91	92	92	93	98	99	98	97	99	98	4	5	10	540	478	672
4	49	M	66	ORIF with asian DCP	80	81	98	81	73	72	70	69	68	66	70	70	81	76	75	73	71	70	70	71	72	97	99	98	97	97	97	98	97	97	100	72	77	80	84	83	80	73	79	80	80	80	82	97	97	99	98	97	97	4	4	10	536	480	689
5	37	M	58	buttress platng with k wire fixaton	86	90	98	87	76	76	74	66	65	63	67	72	90	84	84	83	81	80	79	79	80	99	99	99	97	98	99	99	97	99	90	78	83	96	90	87	85	84	88	89	90	89	90	98	99	99	99	97	98	4	5	10	546	486	692
6	31	M	59	ORIF with asian DCP	79	84	97	80	70	70	69	65	67	69	71	72	84	79	78	77	76	75	74	74	75	99	97	98	97	98	99	98	97	99	105	77	90	95	93	92	90	76	81	82	82	82	84	98	99	97	98	97	98	4	5	10	538	438	684
7	23	F	60	ORIF with plate osteosynthesis	80	95	98	78	71	69	59	78	70	71	72	73	95	90	89	88	86	85	84	85	85	97	99	98	99	98	97	98	99	97	100	74	86	88	87	82	90	86	92	92	93	92	94	98	97	99	98	99	98	4	5	9	498	428	645
8	26	M	55	ORIF with narrow DCP	80	96	99	82	72	72	71	70	70	68	70	71	96	91	90	90	88	87	87	88	88	98	99	99	99	99	98	99	99	98	110	79	90	92	93	91	93	89	94	94	95	95	96	99	98	99	99	99	99	4	5	9	520	439	656
9	33	F	50	ORIF with k wire fixation	89	100	99	90	80	79	77	73	72	70	72	71	100	94	94	93	92	91	90	90	90	98	97	99	98	98	98	99	98	98	90	74	85	95	94	93	92	92	97	97	98	98	99	98	98	97	99	98	98	4	5	10	543	457	668
10	38	M	51	ORIF with asian DCP	89	82	98	87	79	77	75	72	72	71	72	73	82	77	76	75	73	72	71	73	75	97	98	98	98	99	97	98	98	97	100	76	84	85	87	88	89	77	81	81	82	83	83	99	97	98	98	98	99	3	4	8	496	410	630
11	43	F	57	ORIF with plate osteosynthesis	88	97	99	88	77	76	73	67	66	64	68	73	97	92	91	90	88	88	87	88	90	99	97	99	99	97	99	99	99	99	105	76	90	88	89	91	93	92	96	95	96	95	97	97	99	97	99	99	97	4	4	9	521	486	721
12	28	M	56	ORIF with narrow DCP	86	80	98	86	78	77	76	74	73	72	78	80	80	75	74	73	72	71	70	72	74	99	98	98	98	97	99	98	98	99	95	80	80	84	83	78	78	76	79	80	78	79	80	97	99	98	98	98	97	4	5	10	539	468	680
13	29	F	66	ORIF with plate osteosynthesis	80	97	99	81	72	72	71	70	70	69	69	69	97	92	91	90	88	87	87	88	89	98	98	97	98	97	98	97	98	98	120	74	89	91	92	93	96	90	95	96	96	96	97	97	98	98	97	98	97	4	4	9	510	466	674
14	21	M	68	k wire fixation	86	81	99	87	79	78	77	74	72	70	72	73	81	76	75	74	73	72	72	72	73	97	98	99	99	98	97	99	99	97	115	76	87	89	88	90	90	74	79	80	80	80	81	98	97	98	99	99	98	4	4	9	505	460	642
15	46	F	69	k wire fixation	83	98	98	84	78	76	75	74	7	70	75	77	98	92	91	90	89	88	88	88	89	98	98	99	98	99	98	99	98	98	100	78	88	90	87	85	90	90	96	96	97	96	98	99	98	98	99	98	99	4	4	8	514	462	634
16	45	M	68	ORIF with plate osteosynthesis	79	97	98	79	73	72	70	69	68	66	70	70	97	92	91	90	88	88	88	89	90	99	98	98	97	97	99	98	97	99	90	73	78	79	80	82	84	91	95	94	95	96	95	97	99	98	98	97	97	4	4	9	520	474	656
17	31	F	67	ORIF with asian DCP	76	96	99	75	72	70	68	66	69	68	70	71	96	91	90	90	88	87	87	90	90	98	99	98	98	97	98	98	98	98	95	72	76	78	80	85	88	91	94	94	95	96	96	97	98	99	98	98	97	4	4	9	518	447	645
18	50	F	66	ORIF with plate osteosynthesis	89	97	98	89	80	78	77	73	72	70	72	72	97	90	89	89	87	87	87	90	90	96	97	97	97	97	96	97	97	96	130	74	84	90	92	93	94	91	94	93	94	95	97	97	96	97	97	97	97	4	5	11	549	434	677
19	46	M	70	deroofing and curretage	80	97	98	79	72	72	71	70	70	69	69	69	97	92	91	90	87	88	88	89	90	98	99	99	98	98	98	99	98	98	90	74	86	87	94	93	92	90	95	95	96	96	97	98	98	99	99	98	98	3	5	10	538	478	628
20	22	M	60	ORIF	88	82	98	88	79	78	75	73	73	72	71	72	82	77	76	75	73	72	72	75	77	97	99	99	98	98	97	99	98	97	90	80	84	93	94	95	96	78	80	79	80	80	81	98	97	99	99	98	98	4	5	10	560	480	639
21	40	F	70	buttress platng with k wire fixaton	83	97	98	83	75	75	74	73	72	70	71	73	97	92	91	90	89	88	88	89	90	98	98	98	99	98	98	98	99	98	105	80	84	82	78	78	77	91	95	95	96	96	96	98	98	98	98	99	98	4	5	10	570	487	651

S.no	Age	Sex	Wt	Type of Surgery	Baseline PR	MAP	SPO2	Intra op PR 5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	Intraop map5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	intraopspo2 5mt	10mt	15mt	20mt	30mt	45mt	60mt	90mt	EOS	duraton of surgery mt	postop pr 1h	2h	4h	8h	12h	16h	postopmap 1h	2h	4h	8h	12h	16h	postopspo21h	2h	4h	8h	12h	16h	quality	OTSB	OTMB	TDSB	TDMB	DOA
22	41	M	56	ORIF with asian DCP	78	98	97	77	70	70	69	66	64	64	68	69	98	93	92	92	90	89	88	89	89	98	97	97	98	99	98	97	98	98	100	76	85	88	89	88	88	90	95	96	96	97	97	99	98	97	97	98	99	4	4	9	568	490	670
23	50	M	54	ORIF with plate osteosynthesis	72	100	99	73	64	63	61	68	68	70	72	72	100	94	93	92	90	90	89	90	90	98	99	99	98	98	98	99	98	98	95	80	91	93	92	95	96	91	97	98	99	100	101	98	98	99	99	98	98	4	6	12	549	488	683
24	45	F	68	ORIF with narrow DCP	84	101	98	84	74	73	72	69	68	66	69	72	101	94	93	92	90	89	89	90	90	98	98	98	99	98	98	98	99	98	90	78	90	88	85	86	83	91	97	98	98	98	100	98	98	98	98	99	98	4	5	10	620	534	756
25	47	M	69	ORIF with k wire fixation	89	98	98	90	80	78	77	73	72	70	72	71	94	90	89	88	85	85	84	85	88	98	98	99	99	98	98	99	99	98	90	79	88	90	91	87	86	89	92	93	94	93	94	98	98	98	99	99	98	4	6	11	608	512	788
26	40	F	53	ORIF with asian DCP	83	98	97	84	75	74	72	70	70	69	73	74	91	85	84	83	82	80	80	79	80	97	98	97	98	98	97	97	98	97	95	82	90	91	92	93	85	8	88	88	88	89	90	98	97	98	97	98	98	4	5	10	587	491	654
27	38	F	54	ORIF with asian DCP	90	93	99	90	79	78	77	74	72	70	72	73	93	87	86	86	85	84	83	83	85	98	97	98	99	98	98	98	99	98	100	74	78	81	77	76	74	86	91	90	91	92	92	98	98	97	98	99	98	4	5	11	560	486	660
28	21	F	55	ORIF with plate osteosynthesis	92	92	99	91	80	79	78	74	73	72	78	79	92	87	87	86	85	84	83	83	84	99	98	98	97	97	99	98	97	99	95	79	80	82	98	81	80	85	90	90	89	90	92	97	99	98	98	97	97	4	5	10	538	470	643
29	35	M	59	ORIF with narrow DCP	88	95	99	89	78	76	75	74	71	70	75	77	95	89	88	88	86	85	84	84	85	97	98	98	99	99	97	98	99	97	90	80	90	89	88	90	90	86	92	92	93	93	94	99	97	98	98	99	99	3	5	9	537	467	628
30	40	M	61	ORIF with plate osteosynthesis	72	96	99	72	67	65	58	73	71	70	72	73	96	91	90	89	88	88	88	89	89	97	97	98	98	98	97	98	98	97	110	78	84	95	96	95	94	90	94	94	93	94	95	98	97	97	98	98	98	4	5	9	544	472	636